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Anticoagulant Therapy in the Treatment of Thromboembolic Disease

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I AM not going to spend much time reviewing the data on the value of anticoagulant therapy in the treatment of thrombophlebitis. I think the very excellent work which has been done in such institutions as the Mayo Clinic in this country, the twelve cooperating Swedish hospitals in Sweden, and various other institutions throughout the world has adequately demonstrated that in general anticoagulant therapy, if it can be well controlled, is the treatment of choice for thrombophlebitis.

For migratory thrombophlebitis, a disease of a somewhat different nature, one cannot be quite as enthusiastic, but for that matter there is no treatment for recurrent migratory thrombophlebitis that is entirely satisfactory in all cases. Anticoagulant therapy probably represents the best that one can do. As examples of what can be accomplished, several diplomats of world importance today have suffered from migratory thrombophlebitis but have been able to carry on very heavy schedules, following courses of dicumarol therapy for as long as a year to produce complete quiescence of their disease.

The use of anticoagulants in the treatment of coronary thrombosis is a little more recent in its introduction, but data have been accumulating rapidly to demonstrate its importance.

The following data were accumulated by the Committee for the Evaluation of Anticoagulants in the Treatment of Coronary Thrombosis with Myocardial Infarction of the American Heart Association, of which I have had the honor to serve as chairman.

The mortality rate for the control cases of coronary thrombosis treated under fine conditions in 16 of the best hospitals in this country without anticoagulant therapy was 24 per cent. For the cases treated with anticoagulants, it was 15 per cent, a saving of one-third of the lives per attack. When one considers that, in this country, approximately 200,000 people die each year from coronary thrombosis, the saving of one-third represents a potentially significant figure. The greatest improvement occurs in the number of deaths following thromboembolic complications as compared with those deaths which occur without previous thromboembolic complications.

A study of mortality rate per week of illness showed that in each week the number of deaths in the control cases was much higher than in the treated cases. This answers the question: If you do not have the patient to treat until the second or third week is it still worth while? The answer is definitely yes, up to and including the fourth week. After that both control and treated groups have very low death rates.

In the control cases there were 36 complications per 100 cases recognized clinically. In the treated group there were 13 complications per 100 cases, a reduction of almost two-thirds. Actually 5 of the 13 of those statistically located in the treated group were not receiving anticoagulants mostly because they developed complications before anticoagulant therapy was begun. If you deduct these you cut the number of complications down to 8. Therefore, you can say that the incidence has been reduced to one-third or one-fourth, whichever you select. Either

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IRVING SHERWOOD WRIGHT

figure is highly significant statistically, considering that this involves a series of 1,031 cases.

THROMBOEMBOLIC COMPLICATIONS

Patients who develop thromboembolic complications from coronary thrombosis do not all die, but neither do they all escape unscathed; some are left with permanent hemiplegias, some lose a leg through embolism to the popliteal artery, and various other catastrophic events occur. Therefore it is highly important to prevent these thromboembolic complications in addition to maintaining the life of the patient.

All types of thromboembolic complications showed a marked reduction in the treated cases as compared with the control cases. These complications included extensions of the clots within the heart, new infarcts, pulmonary infarctions, cerebral and peripheral emboli, and venous thromboses as in the legs.

If you treat a thousand cases with or without anticoagulants you are going to encounter a certain incidence of hemorrhage. We were surprised to find that 6 per cent of the control cases in our group had some hemorrhagic manifestations, so that all hemorrhages are not necessarily due to anticoagulants. Thirteen per cent of the treated cases showed some hemorrhage, mostly mild. We included in these figures such minor changes as a few red blood cells in the urine or a minor epistaxis.

The types of bleeding were, first of all, hematuria; hemoptysis was more common in the control cases than in the treated group because there were more pulmonary emboli; hematemesis was a little more common in the treated cases; epistaxis did not occur in the control series, but did occasionally in the treated cases. The statistical difference was not very marked except for hematuria.

DICUMAROL THERAPY

We consider fairly optimal dicumarol therapy to be sufficient dosage to maintain a prothrombin time of between 30 and 40 seconds if the control prothrombin time is from 13 to 18 seconds.

We analyzed each complication which occurred because we classified each of these as failures. As a typical example of what we encounter, in one patient the optimal therapeutic level was only reached on one day; at other times the prothrombin level of dicumarol was below 25 seconds, which we consider to be below the therapeutic level. There was progressive extension of the coronary thrombosis together with the development of a mural thrombus, and then death.

In a second case the dose of dicumarol, 300 mg., gave a rise in the prothrombin level to 40 seconds; it was then discontinued, the prothrombin time was allowed to drop below the therapeutic level, and thrombophlebitis occurred in the calf of the left leg.

A third patient was an example of too little and too late. The anticoagulant was never given in adequate amounts to reach a therapeutic level, and the patient died from a secondary myocardial infarction.

In one patient a severe epistaxis occurred early in the treatment with a prothrombin time of about 35 seconds. The question was whether or not it was due to anticoagulant therapy. I probably would have been inclined to discontinue the anticoagulant therapy, but this hospital did continue it; actually it was pretty well demonstrated that the hemorrhage was not due to the treatment alone, because there was no further epistaxis, although much higher levels were ob-

tained. The patient probably blew his nose too hard or picked at it, rupturing a small vessel, and the sealing over was slower because of the anticoagulant therapy.

ANTICOAGULANTS IN RHEUMATIC HEART DISEASE

There is another group of patients who represent an interesting and important opportunity for anticoagulant therapy. These are the patients who have had rheumatic fever and have developed rheumatic heart disease and later auricular fibrillation with multiple secondary emboli.

One patient had rheumatic fever in 1912; by 1941 she had developed auricular fibrillation with mitral stenosis and decompensation. In February, 1946, she had a saddle embolus, and was given heparin for two weeks. The embolus apparently divided and descended downward into the smaller vessels of both legs, but she did not lose her legs. In 1946, between February and June, she had six embolic episodes involving arteries in the legs, the abdomen, and the brain.

In September, 1946, she developed an embolus to the right foot and emboli to both legs. On November 2 she had a cerebral embolus, dizziness, diplopia, slurring of speech, involuntary twitching of the right arm, occipital headache, and lack of convergence of the left eye. Thus she had had a great many embolic episodes, and the outlook was very bad. On November 3, 1946, we started her on dicumarol. She stayed in the hospital for a month under control conditions. Since then (three years) she has been on ambulatory dicumarol therapy and has had no further definite emboli. This woman leads a very active life, and I am very pleased to report that in the three years that she has been free from emboli she has personally raised more than $600,000 to combat heart disease.

A second woman with the same condition might be cited. She developed typhoid fever at 3 years of age, scarlet fever at 4, rheumatic fever at 5, rheumatic heart disease at 6 years, with attacks of chorea at 6, 10, and 12 years of age. She was started on digitalis for fibrillation in 1935 when she was 33 years of age. This patient had twenty-one clinically recognized emboli, following which she was placed on anticoagulant therapy in December, 1946, and remained on the regimen for two and a half years. At that time, having been free from further emboli, she declared a strike and refused to take any more. One month later when she developed a saddle embolus she called me up long distance and said, "I have religion. Come and give me some more anticoagulant therapy. I am never going to stop again." She has led a very active life before and since her last episode, which helped to answer one question which had been hitherto unanswered. This was: Once you place patients who have had many emboli on anticoagulant therapy, when is it safe to discontinue? So far as we know now they must continue on it for life, but at least it will keep many of them alive and active.

The results in this series have been very good.

NEW ANTICOAGULANTS

My past discussion has been largely about dicumarol and heparin. There are, however, some new anticoagulants which should be mentioned. One is a modification of heparin which is now called *depoheparin*. It is heparin in slow-absorbing menstruum. We have found after considerable study that the best way to administer it in general is to give 200 mg. every twelve hours for two or three doses, during which time dicumarol has been started. The prolongation of the clotting time lasts about fourteen to sixteen hours and slowly returns to normal. Each time before giving the next dose it is wise to determine the clotting time by the Lee White method, and before you give the first dose that should be done also. It is advisable not to give another dose if the clotting time is over twenty minutes. If it is below twenty minutes, we give the next dose of 200 mg. It is given intramuscularly.

There is a new preparation called *paritol* which we are now investigating, having administered it to quite a few patients. Paritol works very similarly to depoheparin except that it is given intravenously. The action is prolonged up to eight to twelve hours. We are studying it further from the viewpoint of any possible toxic effects. It is anticipated that if and when it is marketed, it will have the advantage of being approximately one-fifth the cost of heparin. From a practical viewpoint heparin has been difficult to use in large amounts because of the great cost to the patient.

There is also another new preparation known as *tromexan*, which has been developed in Switzerland and has been used there, in Czechoslovakia, and to some extent in England. This is a coumarin preparation which acts like

dicumarol with some added factors of safety. It acts more rapidly; its action subsides more quickly, and it seems more difficult to drive it up to toxic or hemorrhagic levels. These substances will be reported in the literature in the next few months.

Other anticoagulants are also being investigated, but these three seem far enough along now to warrant moderately active studies in man. We have already treated a number of patients with them.

CAUSES OF FAILURE IN ANTICOAGULANT THERAPY

It is always wise to study carefully the causes of failure in medical therapy. We have analyzed these very carefully as they have been encountered in the large national series, and also in our personal experience in consultation work in private and in Army and Veterans Hospitals.

The first important cause of failure in anticoagulant therapy is one which will probably continue to present difficulties. It is the inability to determine the first stages of development of a thrombus. In fact, no matter how skilled we may be as clinicians, it is true that a thrombus probably exists in the veins for hours and, in some cases, a day or two before it can be recognized clinically. During that time, unless we use anticoagulants on a prophylactic basis, the patient does not receive treatment.

The second cause is the delay in instituting anticoagulant therapy after the diagnosis has been made. Frequently there is a period of indecision for two or three days; meanwhile the thrombus is propagating and may well break off and produce a serious embolus.

The third cause is failure to obtain or to maintain adequate levels of effectiveness. A safe scheme for determining the proper level of dosage of dicumarol is the following: First, a control prothrombin time for a given day is taken (perhaps it will be 12 seconds in one laboratory and 15 in another). The ideal therapeutic level is between two and two and a half times the control prothrombin time for that day in your laboratory. That does not mean that you can compare figures from other laboratories exactly, but two to two and a half times is in a good, safe, and therapeutic range. This formula was proposed by E. Sterling Nichol of Miami, and we have found that it is satisfactory.

Another cause for failures is a premature discontinuance of the anticoagulant. Investigation has revealed that many patients who have developed embolic complications have received dicumarol or heparin for four or five days after which it was discontinued. That is wrong. These diseases produce a high mortality in a large number of people—24 per cent in coronary thrombosis—and of those who have one pulmonary embolus from thrombophlebitis, 20 per cent die. When you are dealing with a group of diseases with such a high mortality rate, it is certainly worth while to keep them on anticoagulant therapy for three weeks. Rarely do we discontinue anticoagulant therapy before three weeks, and for cases of coronary thrombosis, we continue therapy for four weeks. If the conditions are suitable this can be done on an ambulatory basis for mild cases of thrombophlebitis after the second week of treatment.

Another cause of failure is the presence of cancer. Any person in the older age group, who develops thrombophlebitis which does not respond to treatment or keeps recurring, should have a very thorough study from the viewpoint of cancer.

We have made a probable diagnosis of cancer in a considerable number of such patients even though the ordinary methods of study have been inconclusive. Later they have proved to have a cancer of the pancreas, the liver, or elsewhere in the body. Study them carefully from that viewpoint.

ABUSES OF ANTICOAGULANT THERAPY

There are many abuses of anticoagulant therapy. The commonest source of abuse lies in the human element—for example, the clinician who administers dicumarol without even taking prothrombin times. We have seen a number of patients who have bled very heavily because they have been given dicumarol with no prothrombin studies and the patient was never instructed to stop taking the dicumarol. One hundred and fifty milligrams of dicumarol a day for a period of time without control will make almost anyone bleed.

Too few prothrombin tests is another cause of trouble. They should be done daily until sure of your patient's tolerance for dicumarol. You can then take prothrombin times three times a week, then twice a week, and finally once a week. It is rarely safe to lengthen the interval between studies to longer than a week. Occasionally you will find a patient whose pro-

thrombin time does not change markedly in a period of ten days on fixed dosage but this must not be assumed.

It is the responsibility of the clinician that the laboratory be accurate. A prothrombin test is not just a routine test. Some physicians have become very morose about this situation, complaining that they could not get their laboratories to cooperate and therefore the whole anticoagulant regimen was in jeopardy. It is generally found that by talking with the technicians and making them realize that they are part of a team that is involved in a life-saving procedure; that they can kill the patients if they report the tests wrongly or carelessly and therefore that it is vital for them to be accurate, most of them will respond and the improvement in many hospitals has been striking. If the laboratory personnel will not accept this responsibility, they must be changed.

We have a standing invitation to the technicians of any hospital. If you wish to have your technician trained in the correct way of performing prothrombin tests and will write to our laboratory at the Cornell Medical College, we will be very glad to arrange for a date for that technician to come to our laboratory for two days, which has proved to be a sufficient length of time for any well-trained technician to perfect the technic.

CONTRAINDICATIONS TO ANTICOAGULANT THERAPY

The physician must know, as in all medicine, the contraindications of the drug that he is using. Hypoprothrombinemia is a definite entity. It may occur without other anticoagulants or dicumarol, as a result of disease, or because of an abnormal status of the bacterial flora in the gastrointestinal tract, thus interfering with the production and absorption of vitamin K.

It is important that patients do not receive anticoagulants in the presence of a marked vitamin C deficiency, but this can be rectified very easily by giving a gram of ascorbic acid in 15 cc. of water intravenously for several days. The fragility of the vessel walls will be rapidly overcome if it is on this basis.

In the presence of marked renal insufficiency, excretion of dicumarol may be impaired. It accumulates, the action becomes more pronounced, and there is some increased danger connected with this. However, if care is exercised, this risk can be minimized.

In the presence of blood dyscrasias with real hemorrhagic tendencies, one must use great discretion. In polycythemia vera it is difficult to control the problem of thrombosis, yet that is what many of these patients die from. However, we have some patients with polycythemia who have been on anticoagulant therapy for several years and have done rather well. It is necessary to watch them more carefully than the average patient.

In the use of anticoagulants in preoperative and postoperative cases one must decide in relation to the individual operation and the patient. For instance, surgery of the brain constitutes in general a contraindication to anticoagulant therapy; also, surgery which leaves wide open areas of dissection. On the other hand, in most general surgery, especially of the lower abdomen, it is possible to reduce the incidence of thromboembolic complications by using anticoagulants.

We consider subacute bacterial endocarditis to be a contraindication to the use of dicumarol.

One should also know that certain drugs affect the action of anticoagulants. These include, for example, salicylates, which tend to prolong the prothrombin time somewhat. Therefore if the patient is taking 40 gr. of salicylates a day he will not require as much dicumarol.

Penicillin is believed to act in the opposite direction. It increases the tendency toward thrombosis, and therefore one may have to give more dicumarol or heparin. Incidentally, some evidence is beginning to accumulate that large doses of penicillin, now given so freely both to medical and surgical cases, do tend to increase the incidence of thrombosis. Statistical evidence is not complete in this regard, but is suggestive and may be an additional indication for using anticoagulants.

Vitamin K compounds, of course, act in the reverse of the anticoagulants of the coumarin series, and vitamin K is used as a definite antidote for marked cases of dicumarol overactivity.

THE proper use of anticoagulants where indicated, for both medical and surgical cases, has been definitely established as a very marked advance in therapy. The present anticoagulants are not completely ideal or satisfactory, but they are the best we have with which to work.

It is reasonably anticipated that from those now being investigated, anticoagulants will be evolved that will be both safer and easier to administer.

Advances in Diagnosis and Treatment of Acute Intestinal Obstruction

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Our discussion is based on the statistical review of cases of intestinal obstruction at Jefferson Medical College Hospital, Philadelphia, and we shall show that the mortality in intestinal obstruction has decreased markedly during the past fifteen years. We believe that this decrease is largely due to the efforts of Dr. Owen H. Wangensteen in educating the medical profession in this particular field. While there are some factors in the management and treatment of intestinal obstruction on which we disagree with Dr. Wangensteen, on the whole we are among his most enthusiastic disciples.

Over a period of ten years, we have gradually shifted to the opinion of Dr. L. A. McKittrick of Boston, that intestinal obstruction is an emergency problem. We believe that the improvement in our statistics is based on this change.

We shall attempt to show that the problems of incomplete, simple, and strangulated intestinal obstructions are almost impossible to differentiate. It is true that the roentgenogram will give us adequate data on the incomplete type, and it is particularly in this type that the duodenal tube and Miller-Abbott tube are most useful. Since most cases of this type of intestinal obstruction occur in the postoperative period while the patient is hospitalized, incomplete intestinal obstruction is very frequently combatted successfully by conservative measures.

On the other hand, complete intestinal obstruction usually occurs weeks, months, or years after a previous operation. In this type, the offending agent is generally a fibrous band which often obstructs a small area of bowel and gives one the impression that he is dealing with an open-loop intestinal obstruction. It is in this particular group that fatalities occur. The roentgenogram may be misleading, and the clinical findings often do not indicate the presence of strangulation until very late in the period.

Case 126 (J. M.) in this series is an excellent example of this fact. Here, the adhesive band caused what appeared to be an open-loop intestinal obstruction, and after a period of four days of conservative treatment, the bowel perforated several inches proximal to the obstructing agent, producing diffuse peritonitis. There were not the usual symptoms or signs of strangulation in this case. The only clue which led to a prompt diagnosis was the rapid rise in the leukocyte count to 22,000. This patient was operated upon with recovery because of the early recognition of the perforation. This case also emphasizes the destructive power of increased intraluminal pressure. The sustained pressure over a period of days was sufficient to produce a focal necrosis and therefore a local strangulating obstruction.

In the second group of cases in which the

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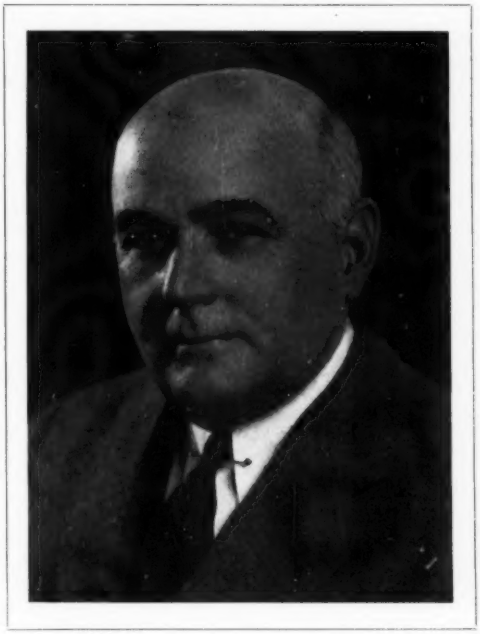
adhesive band plays a very important part, a local necrosis and gangrene are produced by this offending agent. Here again the classical symptoms of strangulated obstruction are lacking. We have frequently encountered a local area of gangrene 2 cm. in diameter with actual necrosis and severance of the bowel wall, except for the mucous membrane. Protracted suction in these cases only leads to disaster and fatality (Figure 1).

Let us review the symptoms of strangulated intestinal obstruction: the initial colicky pain, either with or without distention, depending upon the site of the obstruction; the presence of tenderness and rebound tenderness; and a leukocytosis which may vary from 12,000 to 20,000. The two symptoms of prime importance in the recognition of strangulated intestinal obstruction are tenderness and rebound tenderness, indicative of local peritonitis, caused either by an infarction of the bowel with a chemical peritonitis produced by blood, or by the presence of toxins in the peritoneal cavity because of the permeability of the bowel wall. There is an exception to this rule. Strangulated obstruction can exist without tenderness and rebound tenderness, and this is particularly true in cases of intussusception (Figures 2 and 3).

The disastrous type of case that one encounters is the closed-loop strangulated intestinal obstruction. In our experience, this is most commonly caused by an adhesive band beneath which a loop of bowel is imprisoned. Here, the colicky pain is severe. Early tenderness and rebound tenderness exist because of infarction due to the cutting off first of the venous blood, and subsequently of the arterial blood, causing the associated local peritonitis. There seems to be little excuse for attempting to treat these patients conservatively.

Case 180 (C. G.) from our series is an example of this problem. Here, the patient was treated with morphine and intraduodenal suction for three days. It was not until the patient was moribund that a surgical consultation was requested. Figure 4 shows the pathologic findings at postmortem.

Case 112 (S. W.) is an additional one that was treated medically for seventy-two hours. This patient finally developed tetany. A neurologist, called in consultation, made the diagnosis of intestinal obstruction. This patient had all of the classical symptoms for seventy-two hours. Nothing that I can say or that anyone will write will persuade a mind medically inclined to change to early surgery.



THOMAS A. SHALLOW

In contrast with these 2 pathetic cases, Case 212 (R. G.) was an emergency admission with colicky pain, vomiting, and some distention. She had been ill for fourteen hours. A flat plate of the abdomen showed intestinal obstruction. There was definite evidence of strangulation—tenderness, rebound tenderness, fever, and leukocytosis. The patient was operated upon within two hours, after correction of fluid and electrolyte imbalance and administration of antibiotics. At operation she had a volvulus of the small intestine which required resection of 18 feet of gangrenous bowel. In further contrast, this patient made an uneventful recovery.

Most of our errors have occurred in cases of vascular obstruction. Case 217 (O. G.), a 56-year-old man, was ill for three days with abdominal pain. Morphine was administered by his family physician during this period. Scout films of the abdomen revealed a small area of what appeared to be intestinal obstruction. The diagnosis of mesenteric thrombosis was missed

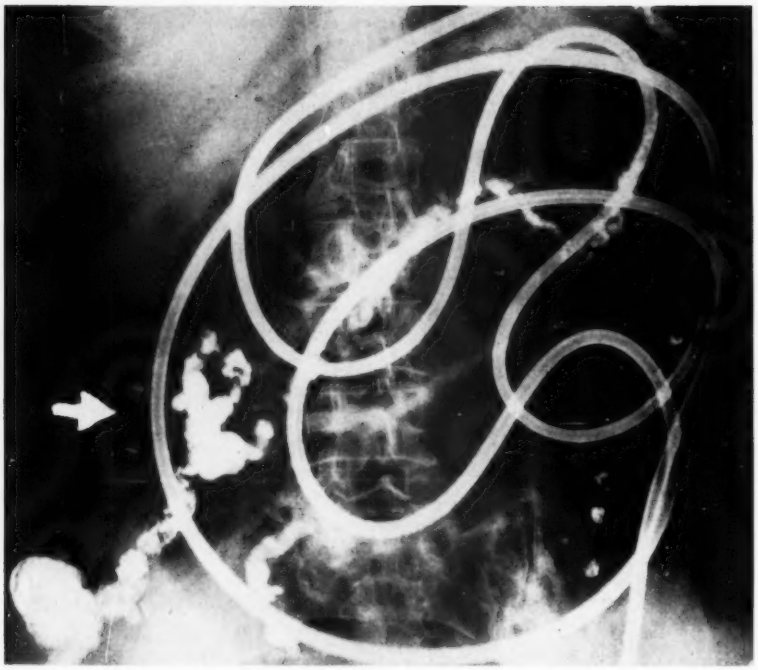


FIGURE 1. Plain roentgenogram, showing distended small bowel in spite of Miller-Abbott tube suction. Delay in surgical intervention for seventy-two hours led to gangrene requiring resection. Patient died three weeks postoperatively. (Case 184; O. W.)

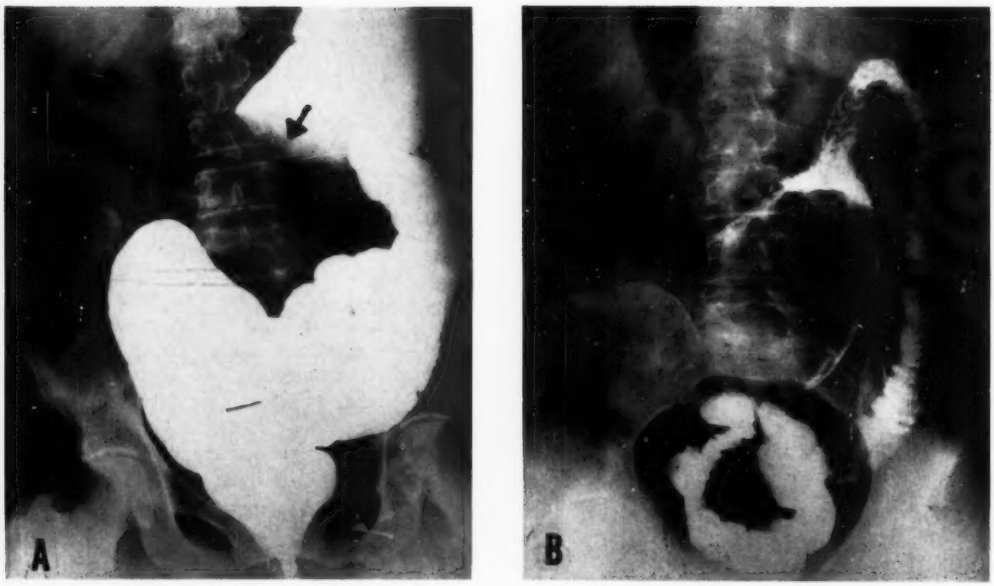


FIGURE 2. Barium enema in case of intussusception with strangulation. Tenderness and rebound tenderness were absent. Arrow in *A* shows complete obstruction at distal transverse colon. Air contrast study in *B* outlines the intussusception. (Case 155; C. A.)

FIGURE 3. Operative specimen of case shown in Figure 2. Arrow indicates carcinoma which caused the intussusception.

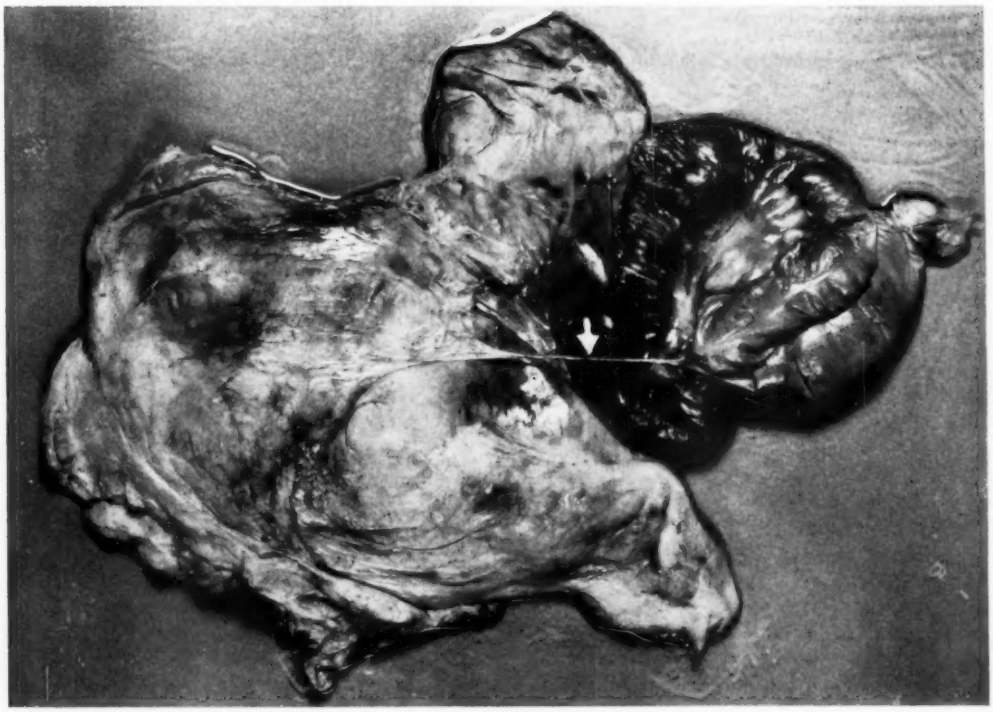


FIGURE 4. Postmortem specimen, showing closed-loop obstruction with gangrene produced by adhesive band indicated by arrow. Early surgical intervention rather than reliance on intraduodenal suction would have saved this patient. (Case 180; C. G.)

FIGURE 5. Gastrointestinal series, showing distended jejunum in case of venous mesenteric thrombosis associated with cholecystoduodenal fistula indicated by arrow. (Case 207; G. M.)

and should not have been because this man gave a typical history of passing blood by bowel two days prior to his admission. He was operated upon as an abdominal emergency, and several feet of small bowel were successfully resected. This patient had tenderness and rebound tenderness, without leukocytosis, and these signs together with moderate distention and the passage of blood should have been sufficient to diagnose the case.

Case 207 (G. M.) illustrates another wrong diagnosis and one which is important to mention. Three months previously the patient had had a gastrointestinal hemorrhage with symptoms of profound collapse, anemia, and the passage of bloody stools. At that time a tentative diagnosis of bleeding peptic ulcer was made and he was transfused promptly with one liter of blood. One week following his admission roentgenologic study failed to disclose any evidence of peptic ulcer. In view of the negative roentgenographic findings, the patient was discharged in the care of a gastroenterologist.

Six weeks later he was readmitted to the hospital with abdominal pain and distention, particularly marked on the left side above the umbilicus. Flat roentgen films showed several feet of distended bowel, and the diagnosis of intestinal obstruction was made. Following our usual policy, his electrolyte and fluid imbalance were corrected, antibiotics were administered, and a duodenal suction tube was introduced.

At operation he had edema of the bowel and its mesentery, with cyanosis and cord-like thickening of all the venous radicals, indicated by a bluish-black discoloration of the blood in this portion of the bowel in contrast with that in the adjacent bowel. The arterial supply was excellent. A diagnosis of venous mesenteric thrombosis was made.

Since knowledge of the cause of venous mesenteric thrombosis indicates that this lesion usually occurs as a secondary manifestation particularly in biliary tract disease, that region was explored. Here we found a hard area which we first interpreted as carcinoma of the gallbladder, since we were feeling across the abdomen from the left side where the original incision was made. A right-sided incision was then made, and after freeing the adhesions, we found that the patient had a fistula between the gallbladder and the duodenum, with a large stone in the gallbladder and stones in the common bile duct (Figure 5). The gallbladder was removed, the fistula repaired, the common duct stones removed, and T-tube drainage instituted.

This patient made an uneventful convalescence, and subsequent roentgenologic study by Dr. Paul C. Swenson showed that the bowel had returned to normal. We have encountered venous mesenteric thrombosis associated with biliary tract disease three times in the past fifteen years, and in the last two instances with stones in the common bile duct.

THE greatest obstacle in delayed operation for intestinal obstruction is distention. Having passed through the period of years before the use of the Wangensteen and Miller-Abbott tubes, and having experienced the high mortality which existed then, we have been fearful of delaying surgical procedure until marked distention is present. While it is true that Dr. Wangensteen[1] has devised a most ingenious method of aseptically decompressing the bowel on the operating table, it is our belief that operation should be done before marked distention occurs, and the Wangensteen method should only be used when the patient comes to us with marked distention.

We prefer to follow McKittrick's plan which consists of decompression until electrolyte and fluid balance are achieved and antibiotics are administered, and then institution of surgical measures. Our reason for reaching this conclusion

TABLE 1

MORTALITY IN ACUTE SMALL BOWEL OBSTRUCTIONS

LESION	1935-1939			1940-1944			1945-1949			Totals		
	Number	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*
Strangulated hernia	10	2	20	15	3	20	45	6	13.3	70	11	15.7
Open-loop adhesive obstruction	5	2	40	16	3	18.8	23	2	8.7	44	7	15.9
Closed-loop adhesive obstruction	1	0		3	1	33.3	9	3	33.3	13	4	30.8
Intussusception	5	1	20	2	0		6	0		13	1	8.8
Volvulus	1	1	100	3	2	66.7	3	0		7	3	42.9
Mesenteric thrombosis	0			2	2	100	3	0		5	2	40
Gallstone obturation	1	0		1	0		1	0		3	0	
Carcinoma	1	0		0			2	1	50	3	1	33.3
Carcinomatosis	1	1	100	0			1	1	100	2	2	100
TOTALS	25	7	28	42	11	26.2	93	13	13.9	160	31	19.4

TABLE 2

MORTALITY IN ACUTE LARGE BOWEL OBSTRUCTIONS

LESION	1935-1939			1940-1944			1945-1949			Totals		
	Number	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*
Carcinoma of left colon	3	1	33.3	10	2	20	20	4	20	33	7	21.2
Carcinoma of right colon	1	1	100	0			5	0		6	1	16.7
Volvulus	0	0		3	2	66.7	3	1	33.3	6	3	50
Intussusception	1	1	100	0			0			1	1	100
Adhesions	1	0		4	1	25	1	0		6	1	16.7
Carcinomatosis	2	0		0			6	2	33.3	8	2	25
Stricture	0			1	0		1	0		2	0	
Imperforate anus	0			1	0		2	1	50	3	1	33.3
TOTALS	8	3	37.5	19	5	26.3	38	8	21.1	65	16	24.6

TABLE 3

MORTALITY IN ACUTE SMALL AND LARGE BOWEL OBSTRUCTIONS

ACUTE OBSTRUCTION	1935-1939			1940-1944			1945-1949			Totals		
	Number	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*	*Number*	*Died*	*Mortality, Per Cent*
Small bowel	25	7	28	42	11	26.2	93	13	13.9	160	31	19.4
Large bowel	8	3	37.5	19	5	26.3	38	8	21.1	65	16	24.6
TOTALS	33	10	30.3	61	16	26.2	131	21	16.0	225	47	20.9

was the failure of duodenal suction by the Wangensteen method to combat distention in low intestinal obstruction. The Miller-Abbott tube which replaced the duodenal tube was equally unsatisfactory, requiring from twenty-four to forty-eight hours before it reached the site of the low obstruction. While it is true that there have been some improvements in the Miller-Abbott tube to cut down this period, we have not experienced this gainful time, and have therefore abandoned it where strangulation obstruction is obvious or even suspected.

Case 184 (Figure 1), referred to previously because of local gangrene produced by an adhesive band, is an excellent example of the danger involved in delaying surgery while relying upon Miller-Abbott tube decompression. Again, the patient was under the care of a medical man for seventy-two hours. When the Miller-Abbott tube finally reached the site of obstruction and x-ray examination showed the closed-loop obstruction present, this patient had gangrene and strangulation. In spite of resection he died of a toxemia three weeks later. I shall not discuss toxemia as a cause of death in intestinal obstruction, because it is still a highly controversial subject.

A statistical analysis of 225 cases of acute intestinal obstruction encountered at Jefferson Medical College Hospital during the past fifteen years is given in Tables 1, 2, and 3. The striking decrease in mortality is attributable to (1) the use of continuous spinal anesthesia in elderly patients; (2) preoperative correction of fluid and electrolyte imbalance; (3) the use of antibiotics, and (4) early operation, using duodenal suction or Miller-Abbott tube decompression as adjuncts rather than definitive therapy.

It is easier to prevent than to cure; early operation minimizes the risks of embarrassing distention, strangulation, and necrosis of the bowel.

REFERENCE

1. Wangensteen, O. H.: New operative techniques in the management of bowel obstruction. Surg., Gynec. & Obst. 75:675-692, 1942.

COMING POSTGRADUATE COURSES

University of Minnesota Medical School, Minneapolis

Continuation course in dermatology, for general practitioners with emphasis on diagnosis and management of common skin disorders, March 27-29. Presentations include psychosomatic aspects, a clinic on dermatologic problems to be presented in University Hospitals, and a conference on diagnostic problems

Continuation course in pediatrics, intended for specialists and devoted to disorders of metabolism and endocrine function, at the Center for Continuation Study, April 10-12. Visiting faculty members will be Drs. Daniel C. Darrow and George M. Guest. Remainder of faculty will be members of the staff of the University of Minnesota Medical School and the Mayo Foundation

Continuation course in gynecology for doctors of medicine engaged in private practice, at the Center for Continuation Study, April 17-19

Continuation course in cardiovascular diseases for general physicians, sponsored by the Minnesota Heart Association, Minnesota State Medical Association, and Minnesota Department of Health, April 20-22

Arranged by The American College of Physicians

Electrocardiography: basic principles and interpretation, at Massachusetts General Hospital, Boston, one week, May 8-13

Endocrinology, at University of Illinois College of Medicine, Chicago, one week, May 15-20

Dynamics of metabolic diseases, at New York University Post-Graduate Medical School, New York, one week, May 15-20

Trends and newer developments in internal medicine, at Temple University School of Medicine, Philadelphia, one week, June 5-10

Internal medicine, at University of California Medical School, San Francisco, one week, June 19-23

Induction of Labor

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The induction of labor may be defined as the stimulation of labor pains by artificial means which usually continue after inception until the birth of the baby. Various forms of stimuli have been proposed and used for this purpose. It may be easy or difficult to accomplish depending upon whether the natural onset of labor in a given case is imminent or remote.

In discussing this subject, therefore, it would seem logical to review what is known about the physiology of the onset of labor under normal circumstances. Our concept of this phenomenon is simple and I will present here the essential facts without going into detail regarding the evidence on which their acceptance is based.

When pregnancy has advanced ten lunar months certain physiologic phenomena occur which bring about the onset of labor.

1. The intrauterine contents have developed to such an extent that strong irritation by pressure is made on the sympathetic nerve ganglia in the region of the cervix supplemented in part by vigorous fetal movement.

2. The placenta at this stage of pregnancy is a senile organ and its ability to manufacture progesterone is markedly impaired, and thus the stimulating action of the posterior pituitary hormone which causes uterine contractions is unopposed. With the fall in the blood level of progesterone there is a rise in the estrogen blood level and this sensitizes the uterus to oxytocic action of the posterior pituitary hormone.

3. Impulses from the pericervical ganglia, reaching the posterior lobe of the pituitary gland via the hypothalamus, stimulate the excretion of its hormone. This causes the sensitized uterus to contract producing more pressure on the cervical ganglia, thus completing the cycle of stimulation which results in labor. (Figure 1.)

How then may we use this knowledge to aid us in the induction of labor? Obviously we must imitate this natural process as closely as possible in order to obtain a normal or near normal response and at the same time avoid certain dangers which may be inherent in the methods which we employ and which might jeopardize the mother, the baby, or both.

METHODS OF INDUCTION OF LABOR

Quinine and castor oil—This is probably the simplest method and depends for its efficacy on the sensitizing action of quinine on the uterine musculature, and the irritating effect of the castor oil on the rectal wall and thereby on the hypogastric plexus. The method is uncertain but not dangerous.

Our method is similar to that of Watson, namely, 5 gr. of quinine sulfate at 6, 7, and 8 P.M. A hot enema is given at 9 and 1 to 1½ oz.

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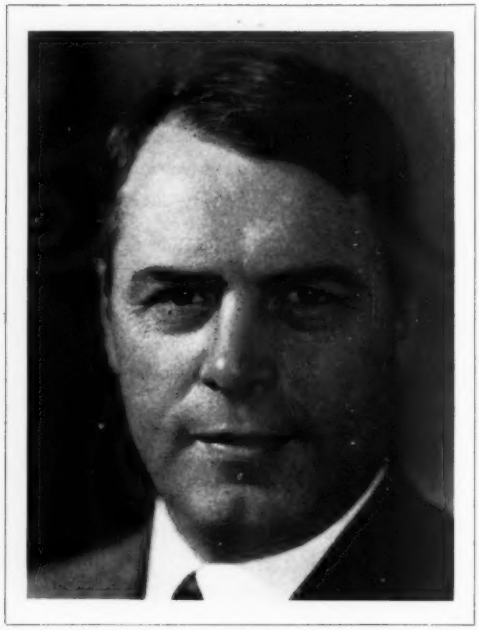
Presented November 3, 1949, before the meeting of the Interstate Postgraduate Medical Association of North America, Philadelphia, Pennsylvania.



FREDERICK H. FALLS

castor oil at 12 midnight. If there are no pains by 6 A.M. minim doses of pitocin are given every half hour until 6 doses have been given. All medication is stopped as soon as pains have become well established. The toxic action of quinine on the fetus has been advanced as an argument against its use for induction of labor. Our experience with the drug has led us to believe quite the contrary, since we have never seen more than ordinary strong pains so stimulated and have had no deaths attributable to this drug as far as we know. The chief criticism of the method as we see it is that the method may fail to stimulate sufficiently so that pains will start and not stop spontaneously.

Introduction of gauze pack or bougie into the cervix of the uterus or the use of the intrauterine bag—These methods are more direct, more powerful, and more dangerous than the former.

The bougie has been largely given up in present day practice because it is uncertain in producing labor, tends to rupture membranes prematurely, may introduce infection into or near the placenta causing fetal infection or possibly producing premature detachment and hemorrhage which would endanger both mother and fetus. (Figure 2.)

The gauze pack is relatively safe but is also less effective than some other methods. Its danger lies in the possibility of the placenta being attached to the lower uterine segment and that it may be partially detached when the gauze is forced through the cervix into the uterus. The technic of gauze induction is as follows:

The cervix is seized with a vulsellum on the anterior lip. The tip of the uterine packing tube is guided to the cervical os by two fingers of the left hand and inserted about 1 cm. through the os. The end of the gauze pack is introduced into the packing tube by the pronged stilette which is then partially withdrawn and pressed forward alternately, carrying the gauze into the uterus and cervix where it acts as a foreign body and irritates the cervical ganglia, thus causing uterine contractions which eventually expel the gauze and later the uterine contents.

The insertion of a Voorhees bag is a valuable and relatively certain method of induction of labor. It is most successful when the patient is just about to go into labor, but powerful enough in its stimulating effect to cause uterine contractions and be effective also before full term.

The direct action of extracts of the posterior lobe of the pituitary gland—Administration of these extracts produces uterine contractions in most cases if given in large doses. The difficulty encountered in this connection is that it is difficult to judge just how much of the hormone to inject in a given case to produce uterine contractions of just the right duration, frequency, and intensity to produce sufficient irritation of the sympathetic ganglia to keep the orderly process of labor going. If too little is given the uterus is insufficiently stimulated. If too much is given the uterine contractions may be excessively strong and long (tetanic) and result in fetal asphyxia due to compression of the uterine artery branches by the contracting uterine muscle as they traverse the uterine wall on their way to the placenta. This may result in intrauterine fetal death, precipitate labor, cerebral injury to the baby, and damage to the soft parts of the mother and may even result in uterine rupture and general peritonitis.

Besides the direct complications that may arise in connection with induction of labor there are many associated dangers which are not frequently encountered but which occur sufficient-

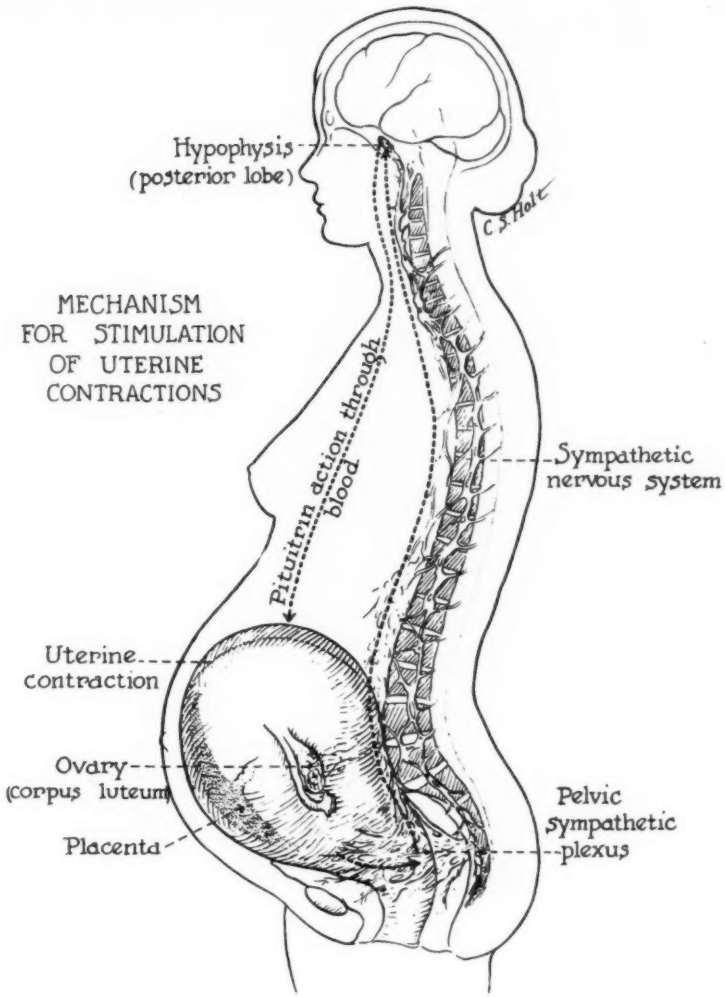


FIGURE 1. Stimulation of the cervical sympathetic ganglia sends impulses through the hypogastric plexus to the hypophysis. The posterior lobe responds by excreting its oxytocic hormone.

ly often to require consideration. Among these may be mentioned (1) unintentional rupture of the membranes during insertion of the bag with consequent potential danger of infection of the amniotic cavity, the placental site, and ultimately the maternal and fetal blood stream; (2) prolapse of the cord in patients in whom the presenting part is high in the pelvis when a Voorhees bag is expelled from the uterus, and (3) very rarely a perforation of the lower uterine segment by the forceps used in the bag insertion occurs. (Figure 3.)

The response may be weak and inefficient, and contractions may stop before or after expulsion of the bag, and often considerable time and nervous energy have been expended by the patient and her relatives to say nothing of the medical personnel charged with her case. Face and brow presentations are said also to be more common in those cases in which a gauze

FIGURE 2. Insertion of pack or bag in such cases would result in fetal death due to laceration of blood vessels or compression of the umbilical cord.

pack or intrauterine bag has been used because of displacement of the occiput by the foreign body. When the bag has been expelled following strong uterine contractions, especially if the fetus is premature—the membranes may rupture immediately and without time for adequate preparation—and precipitate labor may occur. For this reason the progress of cervical dilatation must be carefully followed by frequent rectal examinations to determine as nearly as possible the moment when the bag will be expelled.

INDICATIONS FOR INDUCING LABOR

WHAT then are the indications for induction of labor that are of sufficient importance to outweigh the foregoing dangers and which should be used as a guide to induction?

Eclamptogenic toxemia at or near term which fails to respond to medical management occurring in a multipara with a history of normal labors. These women must be delivered before the toxemia reaches the convulsive stage if possible. Under these conditions the uterus usually responds to stimulation and delivers the baby without undue delay and without injury. If the toxemia is of the fulminating variety, induction is contraindicated and cesarean section becomes the method of choice because of its speed and certainty.

The primipara with a long thick cervix is a poor prospect for induction of labor and should be handled by cesarean section in severe cases or by quinine and castor oil in milder cases followed by Voorhees bag if they respond by softening and shortening the cervix.

In multiparae the danger of bag induction through an unripe cervix is not so great but here too a prepared cervix is an asset which should not be disregarded. (Figure 4.)

Postmaturity, when it seems evident from the history of the case, and the observations during prenatal examination regarding the size and height of the uterus at the various months that there has been no mistake in calculating the time of delivery. This coupled with the evidence of abnormal size of the baby as determined by careful physical examination and x-ray may be a strong argument in favor of induction of labor, especially in a multipara whose previous children have been large and apparently postmature when born.

We prefer to start with quinine and castor oil and if this fails or if only a weak response is obtained, we use pituitrin in 1 minim doses every hour for 6 doses or until pains are established. Larger doses of pituitrin may produce tetanic uterine contractions and should be avoided for two reasons: first, the possible rupture of the uterus; and second, tetanic contractions may interfere with the oxygenation of the fetal blood and intrauterine fetal death may occur.

If medical induction fails a bag induction is indicated. Some obstetricians favor rupture of the membranes in these cases but we feel that other methods are surer and safer because there is less danger of contamination from the intervention.

Closely akin to the postmature baby is the problem of the induction of labor in a patient

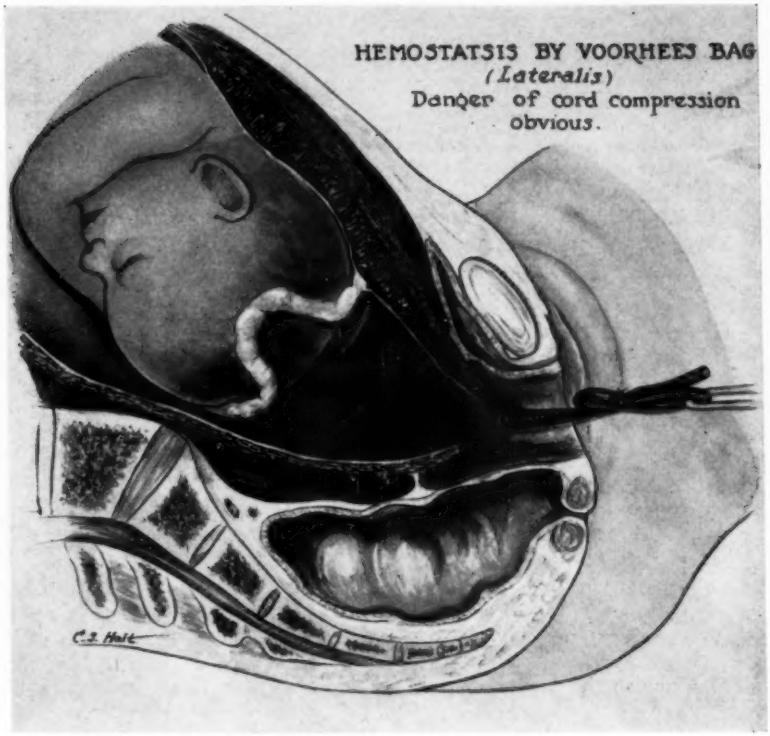


FIGURE 3. Presence of bag causes compression of separated segment of placenta against the uterine wall, stops hemorrhage and stimulates uterine contractions. Danger of cord compression and later prolapse is apparent.

with a known contracted pelvis and especially a multipara who has a history of dystocia due to disproportion in previous labors. Here the problem is complicated by the fact that, if the induction is undertaken long enough beforehand to produce a significant difference in its size, the baby is premature and subject to all the dangers of prematurity plus in many cases an operative delivery from below by forceps or version. In addition, we have a mechanism which is not prepared physiologically to respond to stimulation. For these reasons we are not inclined to do more than attempt medical induction in these cases and failing we await the onset of normal labor and deliver as seems best under the circumstances then prevailing.

Cardiac decompensation of borderline degree may rarely be an indication. In some cases that have cardiac lesions, especially mitral stenosis, acute decompensation develops about the fifth or sixth month of pregnancy. Under these circumstances the patient is put to bed, digitalized and compensation restored in a few weeks to the point that the patient can be up and about but she has little if any reserve cardiac strength.

As pregnancy advances, the upward pressure on the diaphragm and compression of the lower lobes of the lungs embarrasses both respiration and the heart action and signs of return of decompensation occur. Spontaneous labor frequently occurs near term, but this is uncommon before the thirty-second week. The fetus is large enough to survive. Procrastination only results in more decompensation so that stimulation of labor pains is imperative. A medical induction may be tried and if it fails a 6 cm. bag is introduced into the uterus and a 1-pound weight attached. Pains usually start promptly, and the heart stands the first stage of labor very well. In the second stage labor may be terminated by forceps under local anesthesia if it does not end promptly spontaneously.

Induction of labor may be indicated in patients who have diabetes in which cases the

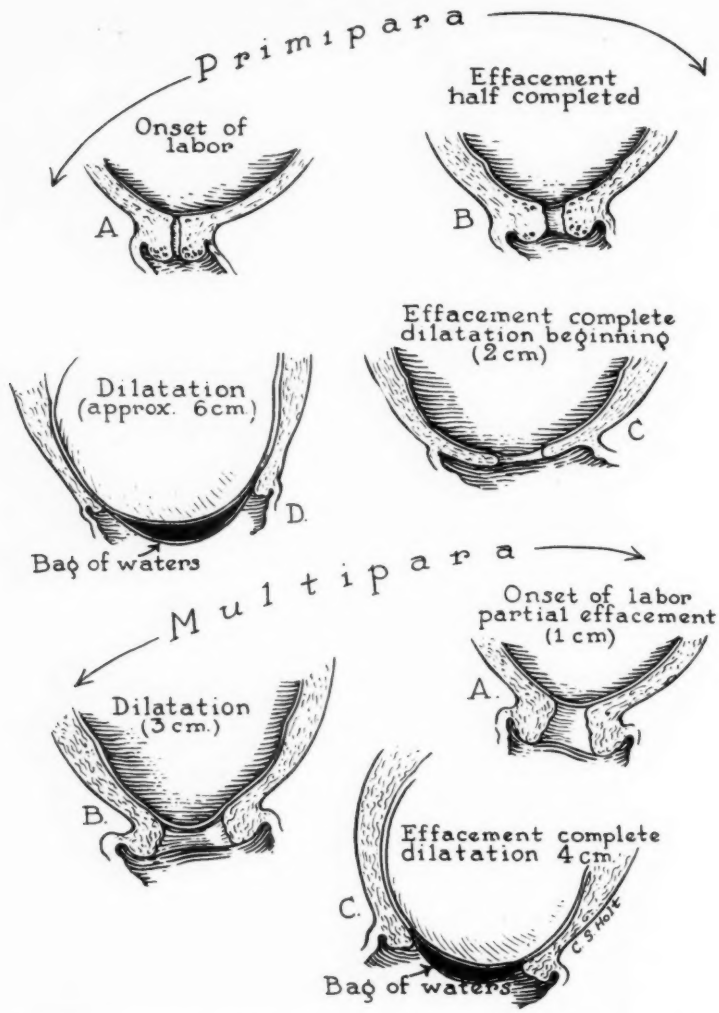


FIGURE 4. Differences in anatomy of cervix explain why induction of labor is more successful in multiparae than in the primipara.

babies are prone to become abnormally large. There are two significant reasons for induction of labor and one against the procedure. The diabetic patient is under an abnormal strain during pregnancy and the sooner this is terminated the better off she will be as far as the diabetes is concerned. Because labor is a function of the endocrine mechanism, it is to be expected that a serious alteration of the function of this system as occurs in severe diabetes might adversely affect the physiologic progress of labor even if the baby is of normal size. As against mechanical induction of labor we have the arguments that diabetics are poorly equipped immunologically to withstand infection and that the danger of induction of labor outweighs its advantage in these cases. However, the fact that we have excellent surgical facilities, antibiotics, and efficient chemotherapy which should be used prophylactically in all cases requiring induction of labor, largely offsets the danger in this respect.

Placenta previa—It is sometimes difficult to decide, when a placenta previa is the problem, how to deliver the case with the maximum of safety to the mother and the baby. Induction of labor must be considered as a possible solution of the problem, but by no means the only solution.

If we are dealing with a central placenta previa there is no argument. The best method of delivery is a cesarean section and as a rule, if the baby is viable the sooner it is delivered the better.

If we are dealing with a lateralis type where the edge of the placenta is only partially over the internal os we are inclined to rupture the membranes and insert a No. 6 bag into the amniotic cavity taking a chance on compressing the cord by so doing. If the heart tones become slow, weak, or very rapid the bag is removed and cesarean section performed. If the lower edge of the placenta encroaches on the lower uterine segment but not in the internal os, we rupture the membranes to induce labor and leave the case to the natural forces of labor. If a bag is not available and the bleeding continues, especially in a multipara with a previable fetus, labor can often be induced and completed most conservatively by rupturing the membranes and doing a Braxton Hicks' version.

TECHNIC OF BAG INDUCTION

THE technic of bag induction may be described in a few words. It is very simple in most cases and we feel that many clinics make too great a fuss over the procedure. In our clinic it is done without anesthesia, although a light gas anesthetic is not contraindicated.

Instruments

1. Twelve ounce syringe which can be sterilized.
2. One vulsellum forceps.
3. DeLee uterine packing forceps. This has a blunt tip and will not rupture membranes.

Equipment

1. Bags #4, 5, 6; larger or smaller bags are useless.
2. Two quart pitcher of lysol (1 to 500 dilution) and basin.
3. Tape to tie stem of bag.
4. One-pound weight attached to cord, and pulley for traction.

Procedure

1. Listen carefully to the fetal heart tones.
2. Place patient in lithotomy position and prepare as for vaginal operation.
3. Fill the syringe and fill the bag with weak lysol solution to test for leaks and carefully note the amount of solution necessary to fill the bag completely. This is the amount to be injected after the bag has been introduced into the uterus when the degree of its distention cannot be observed directly.
4. Fold bag by drawing out the center of the top surface to a point, then fold bag in four layers and grasp with DeLee uterine packing forceps so that the tip of the forceps clasps the tip of the drawn-out part of the bag.
5. Grasp anterior lip of cervix with vulsellum and place two fingers of left hand beneath and to the sides of the cervix. Spread fingers slightly making a groove.
6. Insert the forceps and bag into the groove made by the fingers of the left hand and push it up to the cervix. It is found that it cannot deflect anteriorly because of the vulsellum and the fingers prevent it from slipping posteriorly past the external os so that it is directed into the cervical os and on up into the uterus. If the os is small it may be necessary to dilate somewhat and this can be done easily in most cases by using the tip of the left index or middle finger. Very often the cervix may be soft enough that the bag may be introduced without preliminary stretching.
7. When the shoulder of the bag has passed the internal os of the cervix the packing forceps are removed and the bag is filled, usually with a weak lysol or other mildly antiseptic solution. As the bag expands it is drawn up into the lower part of the uterus displacing upward the presenting part of the fetus. The degree of displacement depends on two factors, the size of the bag and the effacement and dilatation of the cervical os.
8. Immediately after filling the bag to its capacity the operator listens for the fetal heart tones with a head stethoscope. If they are not audible the bag should be emptied immediately. The inference is that the bag in some way compressed the cord and produced asphyxia. This may be due to a low-lying cord or to placenta previa.
9. If the heart tones remain of good quality and normal rate the stem of the bag is folded

on itself twice and tied with a strong tape and wrapped in a sterile towel. In many cases the presence of the bag in the lower uterine segment is sufficient to produce strong uterine contractions in one hour or less.

10. If after a few hours no response is noted a cord or tape is attached to the stem of the bag and led over a pulley so attached to the foot of the bed that direct pull is made on the bag. A 1-pound weight is tied to the string and a similar weight is added if no labor pains are started within another hour.

The degree of progress in the dilatation of the cervix can be evaluated by palpating the bag in the cervix through the rectum, thus avoiding potential contamination of the birth canal. When the bag is about to be delivered through the cervical os it is better if the contents of the bag can be released slowly, avoiding the possibility of sudden expulsion with a prolapse of the umbilical cord.

CONCLUSIONS

1. Labor can be induced in several ways, and depends on irritating the pelvic sympathetic ganglia in various ways and producing a uterine response to posterior pituitary hormone.

2. The nearer the patient is to the onset of spontaneous labor the better the response to artificial stimulation.

3. Certain conditions such as eclamptogenic toxemia and cardiac decompensation predispose to response to the various stimuli used in artificial induction of labor.

4. Bag induction should not be attempted in a patient with an unripe cervix.

5. Contraindications as well as indications exist and each case should be carefully studied before deciding on the advisability of and the method to be used in a given case.

WEIGHING THE BABY
(John Rogus, 1877)
(Courtesy of the New York Historical Society, New York City)

Dynamic Etiologic Concepts

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I DO not propose to waste your time by discussing the textbook causes or so-called "causes" of human disease. I am sure you can do that far better than I. On the contrary, I want to speak to you about the danger of too hurried and too rigid diagnostic pigeonholing which I believe interferes seriously with scientific progress in the field of etiology.

I want to give you, in doing this, a chapter from the experiences of psychiatry which I feel perhaps constitutes the important contribution of psychiatry to the thinking and practice of medicine. I also want to try to give you a kind of philosophical concept which is applicable to the study of human disease of all kinds.

Probably the greatest enemy of straight etiologic thinking has been what I call *post hoc ergo propter hoc* thinking. In effect it means that if two things happen in sequence one after the other, the second is necessarily due to the first. That was the thinking of our primitive ancestors in prehistoric days. When a member of the tribe disappeared from the face of the earth in those dim remote days—and members of the tribe were forever disappearing—no doubt other members of the tribe conferred with each other and said, not in English but by a series of whatever semiarticulate grunts they used, "I suppose you see that he is no longer with us," and the others wisely shook their heads and thought and perhaps some member of the tribe spoke up and said, "He is no longer with us and furthermore did you note that shortly before he disappeared the gods spoke with angry voices in the skies and shot their bolts of warning fire" (thunder and lightning). Then they all sagely shook their heads and said, "No doubt he has offended the gods, he has incurred their disfavor and their displeasure and that is why he is no longer with us."

You may smile at that type of primitive *post hoc ergo propter hoc* thinking. Perhaps you won't smile when I tell you that all of us within your memory and mine have been guilty of the same kind of *post hoc ergo propter hoc* thinking in considering the etiology of human disease. Perhaps I can give you a notable example. Not too many years ago a small group of psychiatrists, noting that a few patients got well after some focus of infection was removed, infected teeth or infected tonsils, then propounded an astounding theory of etiology; they then said that all mental disease, all feeblemindedness, all criminalism, all psychopathic inferiority or epilepsy was unquestionably due to focal infection. You remember that.

Then there came a remarkable thing, an orgy, a kind of psychiatric-surgical debauch which defies description. The psychiatrists and the surgeons joined to remove from human beings

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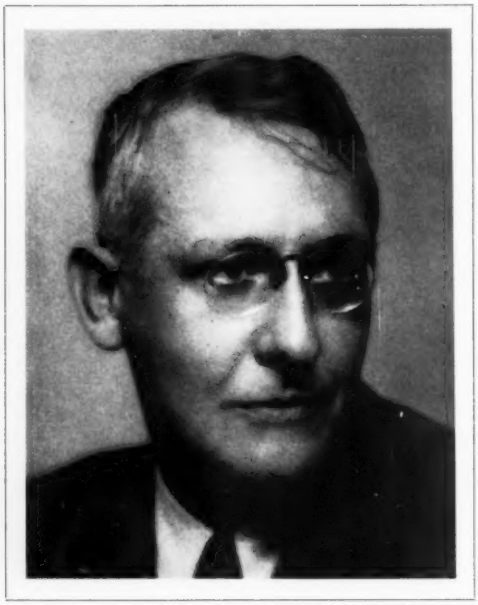


EDWARD A. STRECKER

literally hundreds of thousands of teeth, first infected and then sound, tonsils, cervices, uteri; and then seeking new fields to conquer they began to resect thousands of yards of human colon in the effort to eradicate focal infection and do away with all mental disease. Patients began to die. I remember well at a meeting of the Philadelphia Psychiatric Society my distinguished predecessor, Dr. Mills (and I may say parenthetically that by some good fortune of the gods of science I never joined in this psychiatric-surgery orgy) had this to say: "It seems to me that a considerable number of psychiatrists have joined with their surgical colleagues in a futile effort to eradicate mental disease by reducing the colons of human beings to semicolons!"

You have had your errors in the field of medicine in this kind of *post hoc ergo propter hoc* thinking. You remember auto-intoxication and many other things related to focal infection in your field as well as mine.

The greatest contribution of psychiatry to etiology was a by-product, and the greatest human progress comes not because researchers come to the objective of their research but because of the valuable by-products they turn up in pursuing that objective. That contribution of psychiatry is so great that medicine could not be practiced without it. The entire field of psychosomatic medicine rests on this contribution in the field of etiology of psychiatry, and that contribution, briefly, is something that is no longer a hypothesis but is an axiom; it is the unity of mind-body functioning, the total unified functioning of the human organism.

You know how it was before that occurred—skillful men in all fields, the eye man, the nose and throat man, the internist, the surgeon, looked at a restricted part of man and gave slight if any consideration to the whole man. They did excellent work in their particular fields.

But now psychiatry, probably because it had no instruments of precision, no machine for measuring the integrity of the function of the human heart or the kidney or what-not, probably because it lacked these instruments of precision, had to think, and because it had to think it came across with something which is truly fundamental and without which medicine could not be practiced today—the concept of the total functioning of man.

Briefly, it means, as you know, that in sickness and in health the human being works as a total organism; that, for instance, in sickness a man cannot have a physical process like a fever due to infection without its being reverberated in every recess of his emotional life. If you have any doubt of that, listen to the outpourings of a man who is delirious from fever. Things pour out of his not-conscious mind of which in consciousness he is totally unaware. Contrariwise, a man cannot have anything in his emotional life, either in health or in sickness, he cannot have a mental conflict, an unsolved, unconscious mental conflict, without its being immediately reverberated and profiled in his body. Otherwise, the entire concept of psychosomatic medicine would fall to the ground.

To get back to your practices, a patient will come into your office and tell you what his symptoms are. One man will say, "I have a headache, I am nauseated, I vomit, I have backache," and so forth. There is no magic formula by which at first glance you can tell from what those symptoms have resulted. They may be due to an over-eager celebration at a fraternity banquet the night before; they may be due to a gastrointestinal disturbance of some

seriousness; they may be due to brain tumor; they may be, and frequently are, due to unsolved, unconscious emotional conflict. I said "frequently are" because in my opinion after long years of consulting practice and from the testimony of my confrères in all fields of medicine, not psychiatrists, of every 10 patients you see something in excess of 5 who present the usual symptoms—headache, nausea, vomiting, backache, pains and aches—the symptoms are not chiefly conditioned by disease of structure, inflammation, or degeneration, but are what is called functional; they are the psychosomatic manifestation of unresolved emotional conflict.

Briefly as to psychosomatic medicine, it seems to me that our concept is not as clear as it should be; it seems to me that we are dealing with three levels. The first level probably does not very often enter the realm of disease. It is manifested by an increased activity of function in order to make a compromise as best the individual can make it in groping for a solution of his mental conflict, perhaps cardiovascular overactivity or a great myriad of symptoms which represent an overactivity of function.

Then you come to another level where there are pronounced symptoms; the mental conflict is not solved, and it is necessary for the individual to attempt to find some sort of compromise, so he develops symptoms which take him to the doctor—headache, nausea, vomiting, and a whole host of symptoms. He goes to the doctor because he has become aware of his symptoms.

Finally, in many instances, you come to a third level at which after many years of anxiety and tension, unsolved emotional conflicts become translated into terms of disease of structure. Human function in any of its systems, cardiovascular, gastrointestinal, the skin, whatnot, can only be distorted so long, can only overfunction for a certain period of time and then eventually the tissue breaks down and you have your gastric ulcer or you have your skin condition. There are a whole host of conditions at this third level of psychosomatic concern.

It is difficult to dispose of these things in a short period of time, but I want at least to give you some thoughts or ideas which are applicable to any patient you see, whether it be the schizophrenic or the arthritic, which constitute a kind of philosophy of etiology. Above all, in the practice of medicine we need today a philosophy of etiology, not only in psychiatry, but in all of medicine. Above all, we need to combat sterile, static, pigeonholed diagnostic thinking which serves no useful purpose. It is the way medicine is taught, that the chief objective becomes to fix a diagnostic label—cirrhosis of the liver, malignancy of the stomach, and having done that, the case is put away and, what is sadder, the patient is put away, and what is saddest is that there is then an end to progressive, thoughtful, philosophical thinking concerning the causation of human disease.

Of course we know that the cause of paresis is the spirochete in the parenchyma of the brain. We can diagnose it; we know the treatment; we know the pathology and the neuropathology, but we do not know why of a hundred people who get syphilis, less than 3 per cent get paresis while some of the others get locomotor ataxia and some get aortic insufficiency and others get something else. You can't put a label on a case.

I thought of a jingle which with the permission of the presiding officer I will subject you to:

Little Jack Horner
Sat in the corner
Eating his diagnostic pie.
He stuck in his thumb
And pulled out a plum,
Labeled it neatly and concisely with a diagnosis,
And said, "What a smart boy am I."

Neither you nor I, if we do that, are smart boys, and we are not very intelligent doctors.

I beg of you in this philosophy of etiology to look less at the illness and more at the patient who has the illness. That should be the case not only in my field of psychiatry, but in all human illness. No two pneumonias are the same; no two cases of arthritis are the same; not even any two cases of malignancy are the same, and no two cases of schizophrenia are the same. The important thing is to fix your attention on the person who is sick. Those differences between even common diseases come from a survey of the life history of the person who is sick, so that Bill Smith and John Jones, both having arthritis, present totally different situations.

In my own field of psychiatry I draw an analogy from animals; we should know more about them. How do animals meet the threat to their physical survival which they daily encounter in the jungle? Don't they use those weapons with which nature has endowed them

and which they find most trustworthy in meeting the threats to their survival? There are the poundage animals like the elephant and the rhinoceros who have great weight. When their life is threatened, they meet that danger by charging into it and attempting to annihilate it. Then we come to the great cats, the lions, the tigers, and the panthers; they also have some weight, but they are particularly endowed with tearing power of fang and claw and with feline cunning so that using these they save their lives. Then we come to that interesting animal the possum, the animal schizophrenic who when he is faced with danger to his life plays dead. Then marvelously we come to the great myriads of insects whose lives are constantly in danger, and they save their lives by the power of camouflage which they use every day, and many of them survive because they merge imperceptibly into the bark of a tree, a leaf, or a clod of dirt.

I have been interested recently in studying the three-toed sloth, which is a remarkable animal, and from this standpoint I tell you that there is every reason that the sloth should long since have become extinct. To begin with, the sloth is dim-witted; he is hard of hearing, and his vision is very bad; he moves so slowly that it takes him three weeks to travel two miles; he has no weapons of offense; he spends his life hanging in a tree, and even in his sexual life, at the height or acme of the sexual excitement he often forgets the matter in hand and retires to hang to a tree. This is scientifically true. Furthermore, the sloth is so dim-witted, so hard of hearing, and so half blind that when the baby sloth drops from the body of the mother, to which it clings, to the floor of the jungle, it sometimes gives a weak squeak and the mother very slowly attempts to find her baby, but, again, she can't see well enough; she can't hear well enough; she can't think well enough, and her chances of finding the baby are definitely less than 50 per cent.

Yet the sloth is not only not extinct; it thrives and multiplies and is increasing. It does that because, in the first place, it has a camouflage for merging into the foliage of a tree; in the second place, and very importantly, it eats the kind of leaf in the jungle which all other animals turn away from in disgust, so it has an unlimited food supply; in the third place, it has no body odor, strangely enough.

I tell you that, and it is true, because I am trying to make the lesson that human beings are like animals. When animals are threatened with death they use the weapons with which nature endowed them. When human beings are threatened with psychic dissolution which often results from mental conflicts, they too use those particular weapons of their personality, which in miniature they are accustomed to in so-called psychologic normal health; they construct the psychoneurosis or the psychosomatic situation from the particular things they have in their personality. I wish I could talk more about that.

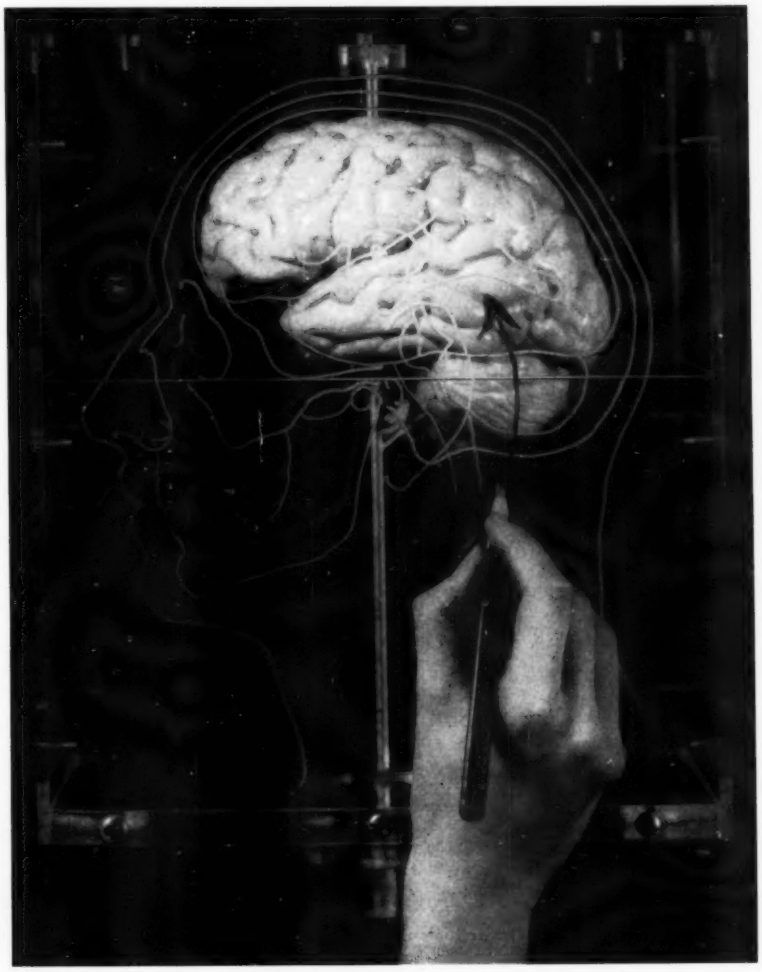
My dear friend the dean of American psychiatry, now Professor at Johns Hopkins, Adolf Meyer, made a very important contribution in so-called psychobiology which is applicable to all human disease. The difficulty was that, being a great scholar, he clothed it in Greek root words and the important meaning was somewhat beclouded by the fact that many of the students did not know just what these Greek root words meant. The nucleus of the concept, psychobiology, is extremely important, and I took from my records one of many cases, giving you only a few high points (there are many others) to show you what Adolf Meyer in his psychobiologic concept meant.

The patient was a young woman who came to me at the age of 21 with schizophrenia. That was a finished maladjustment. These are a few things that happened in her life which may or may not have contributed not only to the schizophrenia but to the particular kind of schizophrenia she had. She was born in difficult instrumental labor at the age of zero. At age 4 she had a head trauma from an automobile accident and was unconscious for a half hour; that may be important. At the age of 10 she had a mental trauma; she was cornered in an alley by a tramp who made this child look at his genitals as he exposed them. At the age of 12 she had her first menstrual period for which she had not been prepared and she was emotionally upset; at first she felt she was going to die when she saw the blood, and then she felt she had committed a tremendous sin. At 15 she broke her wrist, which seems a trivial thing, but she was a girl, the wrist was badly set, and there was a deformity. (I am giving you at random the somatic and emotional impact and insult from the environment.) At 19 she had her only love affair, which terminated unhappily. And very importantly, all through

her life from 1 to 20 she was under the disfavor of her father who much preferred her sister a few years older, and that sister was physically more favored, more alert in her studies, and socially more popular. In the court of the family life the patient was under the stigma of her father. The answer in this case was schizophrenia. In another it might be arthritis or something else.

Finally I call your attention to this formula: P + S ÷ R. *P* means Predisposition to human disease which the individual has gathered in contact with his environment on the red side of the ledger. *S* is the Stress or difficulty that he has encountered in facing emotional stresses, whether acutely dramatic, or long-drawn out. *R*, Resistance, is on the black side of the ledger; it is triumph over environment, the strengthening of the personality from favorable experiences with the environment.

The formula of Predisposition plus Stress divided by Resistance equals what you have before you in a patient. It not only equals what it is, but it equals its severity. That is why in my field schizophrenia might be a simple, mild thing or a malignant schizophrenia. That is why, too, in one tuberculosis case there may be a small twenty-five-cent size lesion at the apex and in another case tuberculosis with Koch's death-dealing bacillus in the blood stream.



Plastic box containing model of brain developed by Illustration Studios of the University of Illinois College of Medicine to permit orientation of the brain to other structures from four points of view.

Diagnostic Clinic

Management of Elderly Patients

EDWARD L. BORTZ*
LANKENAU HOSPITAL, PHILADELPHIA

I AM very happy to present to you five distinguished Philadelphians. Each of these young men is at the summit of his years after a lifetime of very rich and fruitful experience and at the climax of their lives they are in their very prime. Their attitude, in addition to their robust health, guarantees even more years of useful, happy, and interesting living. Each one of these young men is age-ripened and matured, and though past the so-called retiring age, each is continuing to make notable contributions in his separate field.

I want to present to you, ladies and gentlemen, the President Emeritus of Girard College now at the youthful age of 83, Dr. Cheseman Herrick.

Dr. Herrick is a distinguished citizen and he is working on the biography of a noted Philadelphian. He tells me that he will be very busy for the next several years.

Another young man—he is only 72—a distinguished clergyman whose services are widely sought, Dr. Shindel.

Next I would like to present to you a Past President of Rotary International, a lawyer distinguished in many lines of law, who is better now than probably he has ever been in his life—Mr. Glenn Mead. Mr. Mead has no time for retirement; he is going to wait until he gets older.

One of the young men is a former Vice President of the American Medical Association. He told me coming out here that the American Medical Association opened this great auditorium here, Convention Hall, nineteen years ago, and one of the best talks I heard at that time was given by Dr. George C. Yeager. And Dr. Yeager is entirely too busy to retire; in fact, his patients won't permit him to retire. I have been with him on a number of complicated and difficult problem cases, and I want to say now that his acumen and his understanding and his grasp of things medical I assure you will match those of any man I know in medical practice today. He is one of the shock troops in the practice of medicine and is carrying on as he never did before.

Some years ago Dr. John B. Deaver made the statement, in discussing the qualifications of a real doctor, "The real doctor must have the heart of a lion and the constitution of a mule." Therefore, in George Yeager I point to you the perfect example.

I have here a mere youngster, the child of this group of mine here, a distinguished dental surgeon. Dr. Leslie C. Bell is only 70.

When Dr. Bell came into my office, I said to myself in making a preliminary appraisal of the individual, as one does, "Well, here is a man who is probably 50 years of age." When he told me he was 70, I wouldn't believe it. I called in my secretary, Miss Beck, and asked her to check

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with me, and we went into a huddle and made him get out the data, and he finally did prove to us that he was 70 so far as chronologic age is concerned. But let me point out to you the importance of the difference between the physiologic age, which is the real age of the individual, and the chronologic age. They are two entirely different things, and our job is to estimate and make an appraisal of the real age of the individual, that is, the biologic age. It is the biologic age that determines where we stand in our life cycle and determines our future usefulness. The year age, the chronologic age, is a very inexact measure of an individual's life expectancy.

In this field of geriatrics there are many fascinating facets, and we might ask, when is a man really old? I submit to you that a man is old when he ceases to grow; when life's horizons begin to retract, a man is then entering his declining years. As one's dimensions expand he becomes more mature and indeed more alive. As the climax of a play comes in the final act, so should the climax of human life be attained. In the harvest time of a life span, the years of attainment are the years which crown life, round it out to its full completeness, and give it full meaning, extent, and purpose.

For a good many years we have heard of the so-called youth movement that has been popular. It is high time now that an age movement be promoted. The forgotten man in industry today is the man who is entering his mature years. Prophylaxis in this field of geriatrics, in the field of mature years of individuals, may ofttimes be as effective as prophylaxis in the pediatric specialty, the years of infancy and childhood.

EDWARD L. BORTZ

I AM convinced that the most valuable years in the lives of many mature individuals are being lost today due to premature deterioration of the body tissues. Fifty per cent, and probably more, of this deterioration is preventable. Therefore, one of the great problems facing medicine today is to combat the conditions which bring about human deterioration. This is becoming increasingly important because more and more people are attaining the later years of life, due to the magic of modern science.

Should there be a moratorium on the onward march of medical science? What has medical science accomplished in the last half century, in the last quarter century? Think of the discovery of insulin, of the discovery of liver for anemia, or the refinements in our understanding of nutrition, the spectacular drop in maternal and infant mortality, so that these individuals whose lives used to be cut short at the very beginning are now being saved for further experience.

Even in the control of heart disease great progress has been made, and right here I would like to point out to you that when we talk about heart disease as one of the major issues in the later years of life, I submit to you that it is an inexact, inaccurate statement. Heart disease per se may be divided, of course, into four categories: congenital—some of these conditions are receptive to surgery; rheumatic—and now I think we are beginning to see light in the field of rheumatic fever in heart disease; syphilitic heart disease—today nobody needs to die from syphilis of the heart; and, of course, arteriosclerotic heart disease; but here we are in the field of degenerative disorders and that is not heart disease, it is a disease of the circulatory apparatus. We have to sharpen our approach on this because that is the No. 1 major unsolved problem facing medical science today. We hear

a lot about cancer. Well, cancer kills less than 200,000 people a year, but the vascular degenerative lesions kill almost a million people a year. In 1940, 27 per cent of our population were over 45 years of age, but by 1980 probably 60 per cent of our population will be over 45.

While the body strength of individuals may wane in the later years, the mental alertness very frequently sharpens; an individual's understanding and wisdom and the rich quality and texture of the personality only attain their maximum in later years.

You know, you have to be philosophical about this thing, and I submit to you that the mature mind and the wise individual is today the world's greatest need in the field of complex human relations.

One of the most wasteful practices, now considered outmoded, is to retire individuals at the age of 62 or 64. Many individuals are just at their prime then. The increase in the vitality and vigor may go on much later than that, into the later years of life, and the examples are too numerous to mention. Think what would have been lost had Edison been retired at 64. John Dewey just recently celebrated his ninetieth birthday; think of the contributions that he has made to human welfare, happiness, and understanding. Think of Toscanini. I had dinner the other evening with Gene Ormandy, and he told me that Toscanini now is probably doing better work than he has ever done—over 80. Koussevitzky retired at 75 from the Boston Symphony podium so he can go on and develop youngsters in the field of music.

They tell a story about the distinguished Justice Oliver Wendell Holmes, who at 83 or 84 was walking down Pennsylvania Avenue with Justice Brandeis one day. It was in the springtime and a very lovely lady came sauntering down the avenue. These distinguished jurists were engaged in profound discussion of some very esoteric legal matter, but when the Justice saw this beautifully gowned lady his attention was momentarily distracted and he watched her as she kept going by, and after she had passed he nudged Brandeis and said, "Oh, boy, if I were only 70 again."

THE aging of our population is one of the significant challenges of our society today. The many benefits which modern science offers humanity promise a continued extension of the life span. Biologically a race with healthier bodies is the logical outcome, but the social and cultural advantages have yet to be explored. One of the unfortunate limitations that too many doctors follow in the practice of medicine is to limit their interests to the somatic needs of the individual; I think that we should keep in mind that individuals are more than mere bodies and bones and blood vessels; we have to keep in mind that the individual has a nervous system and he has emotions that control his destiny and he has a personality and spiritual makeup. So that I would say that these are the neglected areas in the realm of human relations. Look around you today in the time of the atomic bomb. Possibly we may be facing another Dark Ages period if we become too reckless.

The management of the elderly patient is a challenge to the practicing physician. The type of illness that occurs in people in the later years may be that which occurs in any age; however, the presence of these degenerative lesions of the vascular system, of the heart and the kidneys, and so on, are the ones that should be particularly looked for.

As a football team must be well trained in basic fundamentals, so the basic fundamentals in the handling of individuals, not only in the later years, as a matter of fact, but to keep them well, should be kept in mind. There are four that I am going to discuss with you very, very briefly because I think we are rather naive if we just pass an individual off and say, "Your trouble is due to old age."

One time old Uncle John was sick and he had a sore knee. He called his doctor who had been taking care of him for thirty years. The doctor came in, looked at the knee and said, "Oh, Uncle John, you know that is just due to old age."

Uncle John looked at him and said, "Well, hell, Doctor, the other knee is just as old and it's fine."

Some time ago I made a study of some 200 individuals in the later years of life and found that their diets were deficient in iron, in calcium, and in the proteins, and particularly in vitamin B, especially B_6, the pyridoxine radical. In elderly people—as in other people, but more likely in the later years—there will be a lassitude and a premature weakness and an indifference that develops. All that needs to be done is to make a nutrition survey. Fatigue is one of the

curses of human existence, I suppose, and very frequently I think that in older people the fatigue is due to anemia—just as simple as that. So when you check the blood and keep the hemoglobin well up around 85 per cent and the red cell count around 4,500,000, I assure you that most of the lassitude in elderly people will be passed by.

As to diet, I am convinced that after 50 years of age we should eat more lean proteins, certainly liver three times a week, seafood at least once a week, with a marked restriction in fat and a moderate restriction in carbohydrates, but let's take more iron and proteins and the vitamins, particularly vitamins A and B.

Secondly (and how simple this is), elimination of waste products. The doctor has to keep in mind that the bowels, the kidneys, the skin, and the lungs should be well cleared out, because the fire of life burns more brightly when the heater is not clogged with ashes.

Third is rest. These are all very easy, but oh, how neglected they are. Sometimes I see patients that have been giving themselves tonics and what-not, when really they have not been getting enough rest or have been on a poor diet; it is as simple as that.

When we talk about rest we do not mean the thing you get from the poison of a barbiturate or amytal or something like that, but sufficient, complete, and adequate rest of the physical body, the nervous system, and the emotions which will help a lot in getting rid of the depressions of old age; the weariness of elderly folk which may produce mental sluggishness may be greatly alleviated by adequate rest. Many times older folks do not require as much sleep as they needed in the earlier years, but that is a personal detail. An invaluable practice is the afternoon nap following the lunch hour. This is a most useful practice and I would recommend it to you doctors—I have tried it myself occasionally. After all, though we may be so very impressed with our own importance, no one amounts to much as one individual; so I think if we would not take life too seriously that would be one of the crowning balancing influences.

The fourth standard requirement is recreation; rehabilitation, which eliminates fatigue, keeps the mind and the body clear, and invites a new point of view and prepares the individual for the next day's work. Therefore, to develop an avocation which may be followed as often as possible, certainly through the week too, is essential to balanced living. And aren't we interested in balanced living?

Some years ago Richard Cabot wrote a book on What Men Live By—Work, Play, Love and Worship. The balanced individual has to have a work that will give him significance in the social fabric.

Security is a term which is much in the public mind at the present time. Old age assistance is a matter of national concern. To solve the problems of the later years of our aging population, a much broader approach than merely financial contributions must be found. To make the lives of our older fellow-citizens socially significant, each community should promote those measures which in addition to improving the health will utilize their talents and experiences in industry, field, and school. To be gainfully employed makes the lives of our elderly citizens useful and banishes the need for financial contributions from the public treasury. The artificial barriers to the employment of older men and women should be completely eliminated.

A program for the continued education of elderly men and women will create new vistas and fields of interest that may lead to important accomplishments. There are many examples. Cato began the study of Greek when he was 80. Sarah Bernhardt with a wooden leg gave one of her greatest performances when she was 77. Grandma Moses found herself in the field of art after so many of her friends had been retired.

The creation of geriatric clinics is a very important need today. With the establishment of these clinics we will focus attention on the overall needs of the individual in the mature and significant but neglected years. The medical profession should exercise real leadership. Doctors should keep their patients physically healthy and emotionally tuned up, and then they should help to see that they are gainfully occupied.

As the wear and tear processes produce breaks in the efficiency and ability of oldsters to carry on, satisfactory homes must be found. If it is within the family circle, all right, but ofttimes—and we notice this in the metropolitan areas, too—the older folks may be beyond the period of ordinary activity and participation in the life of the family, and, if we are not careful, all of the assets and resources of the family may be dissipated.

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For these individuals, the wholesome thing to do is to create institutions where they may associate with individuals at the same period of life and have their needs taken care of by professionals. Far from being unkind to a parent whose care in the waning years may exhaust the family resources, it is wise to place our loved ones in a home for elderly folk where their needs are the chief responsibility of a trained staff and where they may be taken care of perfectly adequately.

More and more of these institutions are being established in communities where an enlightened attitude toward the management of elderly individuals has been given serious thought.

Management of the elderly patient is a challenge to each of us as physicians. Age has its triumphs no less than youth itself; the problems of the later years are not confined to medical needs. The social implications are far-reaching and the cultural needs likewise are pressing today for solution. These problems are fascinating. Indeed, as we look around us and see the antics and performances of individuals, aren't we impressed with the fact that there is a lack of maturity, of emotional maturity? Individuals with strong backs and weak minds make up entirely too large a proportion of our population. The problems of the later years give the physician opportunity to extend the horizon for each of his elderly friends. The physician needs to care for the physical requirements, but he must find ways and means to prevent, when possible, the signs of age in his older patients; he has to practice preventive or prophylactic geriatrics.

To be a physician for elderly folk affords one rich and rewarding experiences. I first became interested in this problem with my own beloved father when he had turned 60 and the shadows were lengthening. I remember when I looked at him and said to myself, "Daddy, you are an old man," and then we did something about it. We had a very rigid critical physical survey and then we studied him from the total point of view, and inside of two or three months he took on new life, and I tell you that the last eighteen years of his life (he lived to be almost 78), the geriatric years, were the years of his greatest enjoyment, I think.

So we have to be philosophers in this business of practicing medicine, and we doctors have to set our eyes on the far horizon. Beyond philosophy, the spiritual adjustment of our patients becomes important, and in this sphere of religion there is often found for our elderly friends a peace of mind which is beyond understanding.

I have been delighted to have my good friends, these distinguished Philadelphians, come here and serve as guiding lights and examples to show you young men at the summit of their years, who are looking on into the future with a firmness and a belief in themselves and a love for their fellowman that is finer and greater than they have ever known before.

SPIES AND WILLIAMS RECEIVE CUBAN AWARD

Two outstanding nutrition experts, Dr. Tom D. Spies and Dr. Robert Williams, recently received the Orden de Carlos Manuel de Cespedes decoration, highest award of the Cuban government.

Dr. Spies, professor of nutrition and metabolism and chairman of the department in Northwestern University's Medical School, was cited for his contributions to the field of nutritional deficiency disease. Dr. Williams, formerly chemical director of the Bell Telephone Company laboratories, was honored for his work in isolating vitamin B_1, analyzing its structure and producing it artificially.

Backed by Northwestern University and the Spies Committee for Clinical Research—business and professional leaders interested in the doctor's work—a campaign is now underway to create a world center for nutritional research in Chicago to be directed by Dr. Spies.

Diagnostic Clinic

Diagnosis and Treatment of Hodgkin's Disease

ANTONIO ROTTINO*
ST. VINCENT'S HOSPITAL, NEW YORK

The nature and etiology of Hodgkin's disease remain today as mysterious as was the case in 1865 when Wilks named the new syndrome after his predecessor, Thomas Hodgkin.

By 1904 the pathology of Hodgkin's disease had been adequately described, and little has been added since. Bacilli, fungi, parasites and viruses have at various times been suspected of being the causative agent. In 1943, Grand, using the tissue culture technic, revived the virus theory. Neither Hoster nor I was able to corroborate Mr. Grand's tissue culture findings. For the time being there is no critical evidence as to etiology.

The pathologic alterations found in this disease are of a mixed nature. Some of them stamp it as neoplastic, while other alterations are definitely inflammatory in nature. On the basis of our personal observations gleaned from rather extensive clinical and pathologic material, we incline more and more toward the neoplastic theory.

I should like at this point to discuss some phase microscopic studies which have tended to influence our opinion in this direction.

The pathognomonic cell in Hodgkin's disease (Figure 1) is a large reticular cell with abundant cytoplasm (a), a single large round nucleus and a prominent nucleolus. Examination of the following reticular cells (b), with indented nuclei (c), pleomorphic nuclei (d and e), multiple nuclei, illustrate clearly the histogenesis of the Sternberg-Reed cell from this type of reticular cell (a).

In addition to the abnormal reticular cell which finds its most conspicuous expression of physical alteration in the Sternberg-Reed cell we find in certain phases of Hodgkin's disease hyperplasia of lymphocytes, proliferation of normal-appearing reticular cells, infiltration with eosinophiles, proliferation and swelling of vascular endothelium, necrosis, and fibrosis. All these latter changes we consider reactive phenomena secondary to the metabolic aberrations which undoubtedly accompany the abnormal physical alteration of the reticular cells just referred to in Figure 1.

I shall now discuss briefly and demonstrate with illustrations the various modes of onset of Hodgkin's disease which should be kept in mind when attempting diagnosis.

Probably the most common symptom of Hodgkin's disease is swelling of the neck (Figure 2). Here we have a typical instance; a patient who discovered while shaving one morning that his neck was enlarged. The day before the swelling had not been apparent. Sometime the swelling develops and appears even more quickly. As illustration, a mother sent her child to a St. Patrick's day parade, washing his neck thoroughly while dressing him and noting nothing abnormal. When the child returned later in the afternoon she noticed swollen nodes in his neck; the next day they had grown so in size that she came to the hospital for advice.

In still another instance swelling in the neck was acute, rapidly became diffuse and simulated cellulitis. During operation for cellulitis no pus was found, the patient's condition became seri-

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ANTONIO ROTTINO

ous, the operation was terminated and no diagnosis made. A few days later nodes appeared in the axilla and from then on the diagnosis was more obvious, and subsequently established.

Although Figure 2 is of a lymphadenopathy localized in the neck it should be stressed that such a cervical lesion may be only a part of a general lymphadenopathy. It might be well to stress too that often localization of Hodgkin's disease may be evident at sites other than the neck—in the axillae, one or both groins, etc. I remember the case of a young girl who while cleaning the stairs tumbled down them; when examined by a physician a swelling in the groin was noticed and a diagnosis of hernia made. She was operated upon and a node was found which was later diagnosed as Hodgkin's disease. For some reason or other this patient received compensation for a supposed hernia for over a year.

In other instances the disease expresses itself in symptoms referable to the lung or the thorax.

A young person came to the hospital with fever and his chest plate showed presence of a pulmonary mass which was interpreted as tumor (Figure 3). Some time later a node made its appearance in the neck, biopsy of which node established Hodgkin's disease.

Another type of onset is illustrated by a patient (Figure 4) who entered the hospital with fever, sweating, and this large shadow. These symptoms were variously interpreted as tuberculosis, virus pneumonia; only sometime later when a lymph node appeared from which a biopsy could be done was it possible to establish a diagnosis of Hodgkin's disease.

Mediastinal enlargement is shown in Figure 5. The patient from whom the x-ray was taken was conscious of no trouble whatever. The findings were made during a routine examination by a military board.

Figure 6 shows the actual appearance of a lung with nodules of the type which give the x-ray shadows just shown.

THE next series of illustrations show the gross pathologic appearance of enlarged nodes producing the x-ray shadows just described.

In Figure 7 you see the lungs, heart, and mediastinal enlargement continuous with a cervical mass.

Figure 8 is a picture of a lymph node in the hilum of the lung, showing the bronchus and the hilar nodes.

Now and again Hodgkin's disease will at first exhibit symptoms apparently indicating an obscure ailment, with splenomegaly. The splenomegaly may be the only finding, or it may be associated with anemia, purpura, leukopenia.

In one instance the patient entered the hospital because of severe anemia. The only physical finding was an enlarged spleen (Figure 9). When this was removed, we found to our surprise that it was the seat of Hodgkin's disease.

Another way in which Hodgkin's disease may make its appearance is illustrated in Figure 10. This patient was followed in the eye clinic for almost two years for proptosis. In addition to the proptosis he had a small node in the neck to which scant attention was paid. Finally the node was removed, and a diagnosis of Hodgkin's disease was made. When nitrogen mustard therapy was instituted the proptosis disappeared proving that the pathology behind it was Hodgkin's disease.

Still another way in which Hodgkin's disease sometimes becomes clinically manifest is by backache. This may or may not be associated with changes in the vertebral column such as

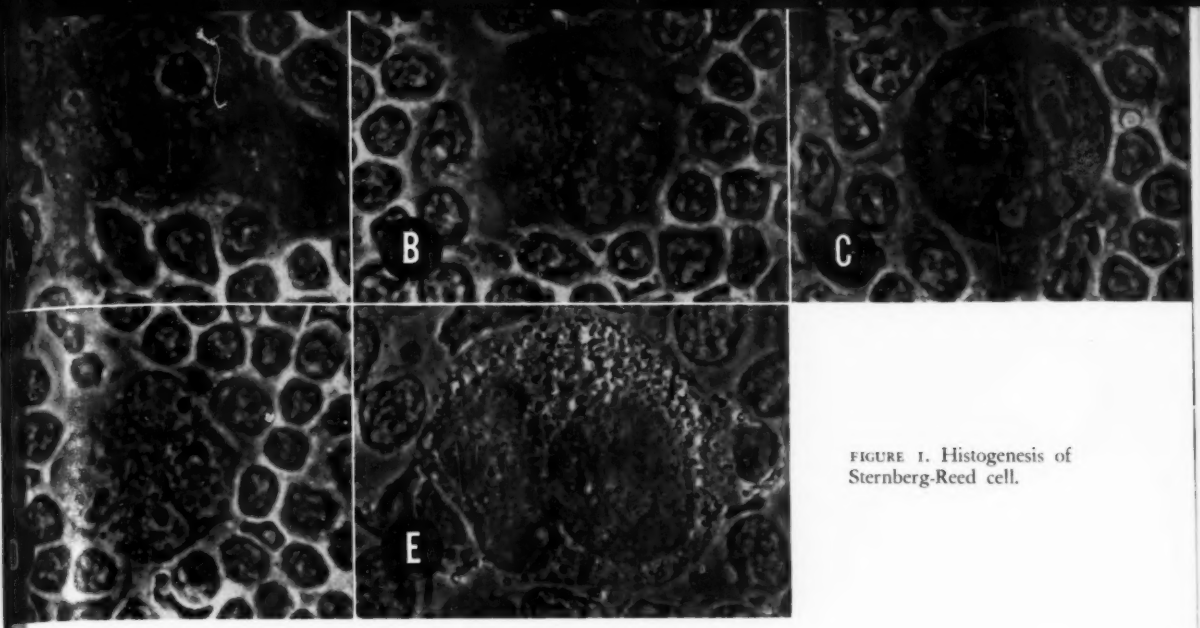


FIGURE 1. Histogenesis of Sternberg-Reed cell.

are shown here (Figure 11). The interpretation is not infrequently "metastatic tumor." Often the backaches are ascribed to arthritis.

A very common way in which Hodgkin's disease manifests itself initially is by pruritus (Figure 12). This particular patient had pruritus for almost four years and went from doctor to doctor, receiving various diagnoses and treatments, one of which deprived her of portions of her diet. In the meantime her skin became transformed as you see here. She had only one lymph node in her neck, and about 95 per cent of it was fibrous tissue which made diagnosis difficult. The subsequent course and another biopsy finally made a diagnosis of Hodgkin's disease possible.

Another onset is characterized by fever (Figure 13). Any obscure fever can be suspected of indicating Hodgkin's disease. Very often persons with this symptom are diagnosed as having miliary tuberculosis, subacute bacterial endocarditis, etc. This particular individual was followed for a month, during which he had very high fever, 104 degrees, and a relatively slow pulse. Only one lymph node ever made its appearance and from it diagnosis was established.

So much for the onset; now let us consider the clinical course. This I have divided into three groups: (1) acute, (2) chronic, (3) chronic and protracted.

Difficulty is encountered in the classification of the acute cases because often it is not easy to determine the date of onset of the disease. Experience has already taught us that patients who seem at the time they first visit us to be suffering an acute attack of some rapidly-progressing disease have as a matter of fact been afflicted with Hodgkin's disease for years, the symptoms having been so mild as to have been either disregarded or diagnosed as "flu." Actually the acute picture represents in these cases the terminal phase of a long-standing disease.

The acute cases are luckily relatively rare. Only five per cent of our entire group were acute. By acute I mean those cases which from the very onset are febrile, run a very rapid course, and end in death at approximately six months, and in which x-ray and nitrogen mustard therapy are ineffective. Associated with the acute phase there is usually depression of all the blood cell elements.

The so-called chronic cases constitute the larger group, forty per cent. The course runs from one to five years. Their initial response to therapy is good. They have frequent remissions, frequent relapses, and are prone to most types of complications, which I shall illustrate.

FINALLY we have the so-called chronic and protracted cases that go on living for six years, seven, fifteen and even thirty-five years. They respond very well to the initial therapy, and following the therapy remissions occur which may last from five to six or seven years without any further therapy.

Table 1 shows the overall picture in Hodgkin's disease. Seventy-two per cent of the patients are usually dead within three years; twenty-eight per cent live longer.

FIGURE 2. Swelling left neck due to Hodgkin's disease.

TABLE 1
DURATION OF LIFE IN YEARS

YEARS	CASES	PER CENT
1	15	
2	14	72
3	16	
4	4	
5	5	
6	1	28
7	4	
8-15	3	

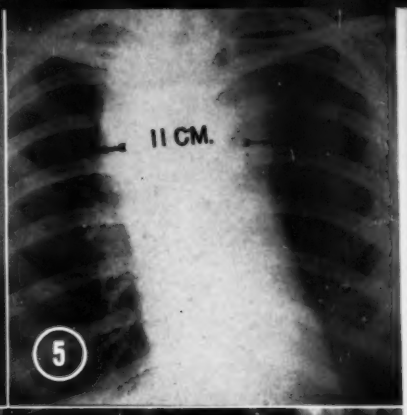
Let us next consider some complications that occur in the course of Hodgkin's disease. I shall first discuss types of lung change which we have encountered. These may occur early or late in the course of the disease, they may regress, or they may continue and become disseminated. Usually the complications occur quite late.

Figure 14 shows a lung in which numerous discrete masses are seen throughout the organ.

An example of bronchial involvement may be seen in Figure 15. Note the nodularity of the mucosa. The individual from whom the specimen was obtained died from heart failure before the Hodgkin's disease had time to run its full course.

A very curious complication was encountered in one individual who, after drinking some milk suddenly began to cough it up. Subsequent x-ray studies demonstrated the passage of barium from the esophagus through a bronchus into the bronchial tree. We have seen this just once. The x-ray plate (Figure 16) shows the barium in the esophagus and trachea.

Pleural effusions are very common. Figure 17 illustrates the appearance of the pleura at autopsy in an individual who had pleural effusion. Notice the distribution of these irregular masses over the parietal pleura and diaphragm and also on the vertebral column. Not infrequently



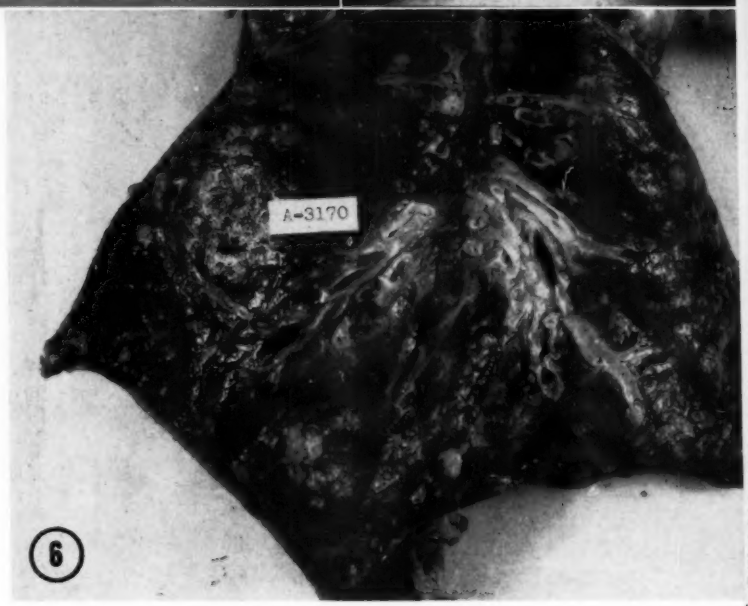


FIGURE 3. An intrapulmonary mass simulating a lung neoplasm, due to Hodgkin's disease.

FIGURE 4. Diffuse shadow left lung field simulating tuberculosis or virus pneumonia, due to Hodgkin's disease.

FIGURE 5. X-ray view of a widened mediastinum due to Hodgkin's disease.

FIGURE 6. Lung containing multiple nodules. These are typical lesions of Hodgkin's disease.

these masses extend through the vertebrae into the spinal canal.

Jaundice is a complication occurring in Hodgkin's disease. Most often the jaundice is due to large lymph nodes compressing the bile duct, causing obstructive jaundice (Figure 18).

Amyloid disease complicates about three per cent of the cases of Hodgkin's disease.

Occasionally Hodgkin's disease produces a frozen pelvis due to involvement of the lymph nodes in this region. Now and again large lymph nodes in the pelvis compress the ureter and produce a hydronephrosis.

Enlarged abdominal nodes may compress the aorta, causing marked constriction (Figure 19).

Acute pancreatitis may complicate Hodgkin's disease. As a rule, it is a terminal event.

Edema of the arm, such as you see in Figure 20, may occur, and it sometimes persists for two years before the patient dies.

An individual with marked edema of the breast is shown in Figure 21. Subsequently she developed edema of the arm and of the lower extremity. In another patient a large mass developed over the sternum, pointing outward.

Skin nodules are sometimes seen.

Purpura may develop (Figure 22). This is associated with a thrombocytopenia.

Now and again we find in these patients a herpes zoster. Herpes zoster may occur any place on the body; in this particular instance (Figure 23a) it was on the inner aspect of the thigh. These usually heal completely but in an occasional case, if it has been severe, scars may remain (Figure 23b).

Now and again the patient develops abdominal swelling and ascitic fluid is suspected, but experience has shown that very often the swelling is due to large masses (Figure 24) in the upper abdomen which involve the lymph nodes of the mesentery and about the pancreas and which push the liver and stomach forward.

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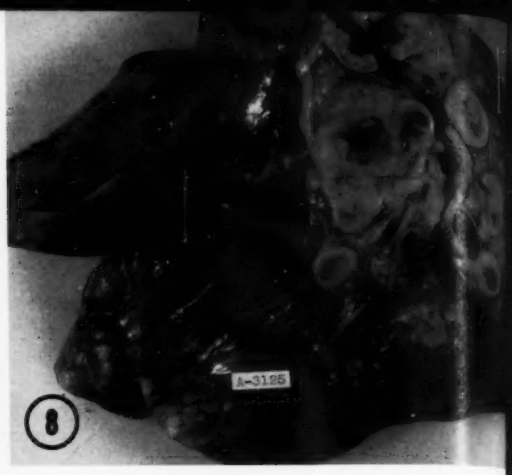


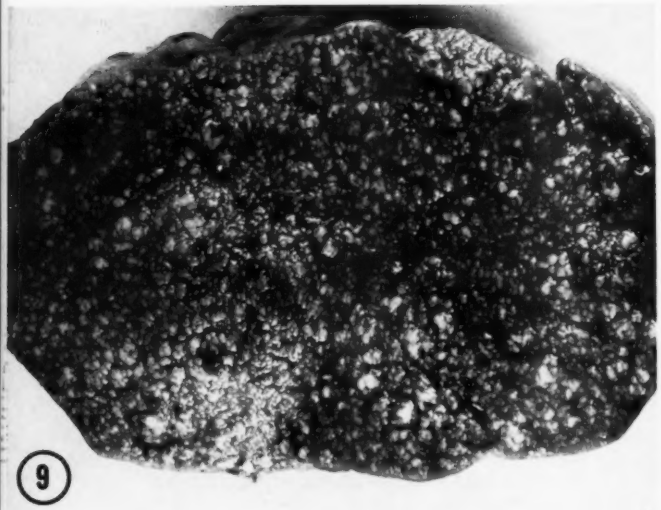


FIGURE 7. Actual appearance of enlarged nodes in the mediastinum responsible for x-ray picture such as is seen in Figure 5.

FIGURE 8. Enlarged hilar nodes due to Hodgkin's disease. These, on x-ray, simulate shadow of a primary bronchial carcinoma.

FIGURE 9. Typical porphory spleen of Hodgkin's disease.

FIGURE 10. The left eye protrudes, due to Hodgkin's disease behind the left eyeball.

FIGURE 11. Vertebral bodies; note grey mottled areas representing replacement by Hodgkin's tissue.

FIGURE 12. Skin markedly wrinkled, thick, rough and dry due to chronic pruritus.

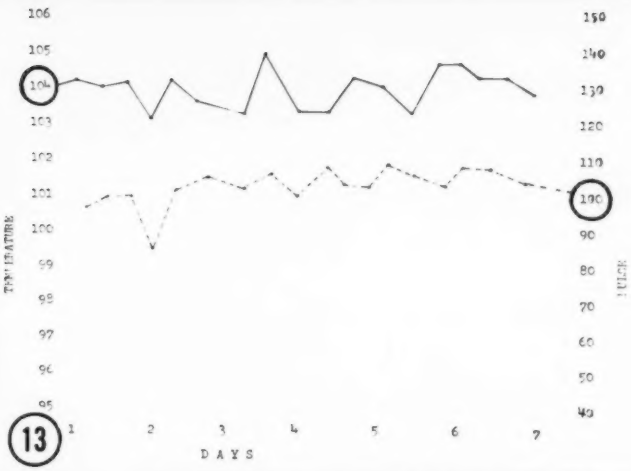
FIGURE 13. A typical febrile reaction of patients with Hodgkin's disease.

FIGURE 14. Lung with multiple nodules due to Hodgkin's disease.

FIGURE 15. Right main bronchus containing multiple nodules due to Hodgkin's disease.

FIGURE 16. X-ray showing a broncho-esophageal fistula. This is a rare complication of Hodgkin's disease.

FIGURE 17. Pleura studded with multiple nodules.



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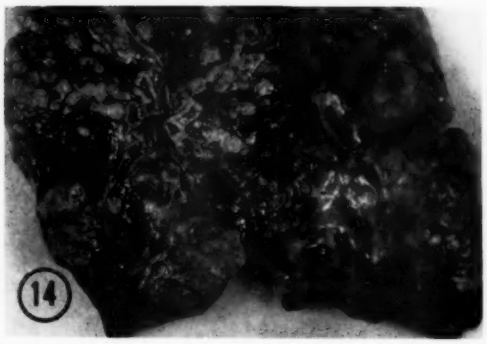

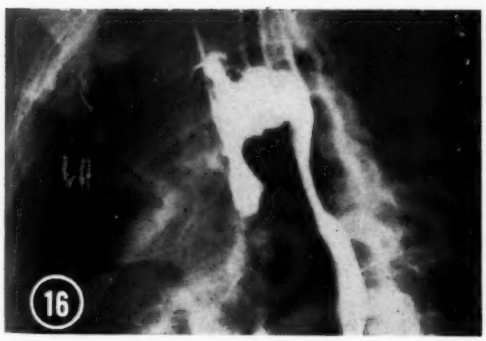

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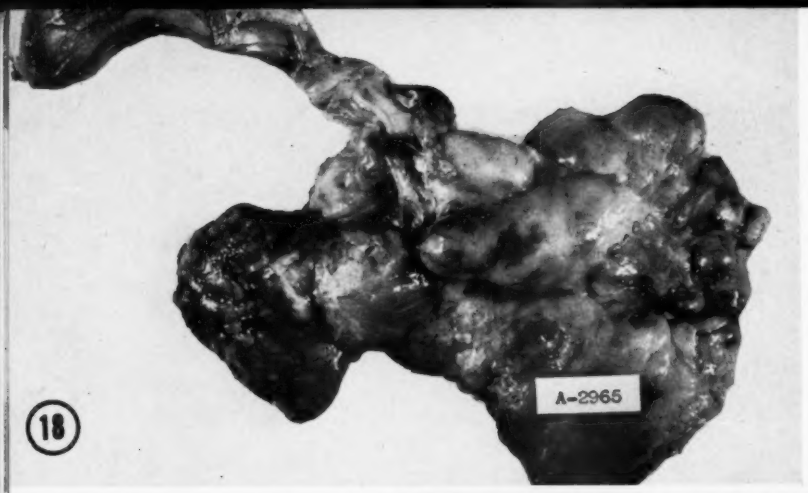
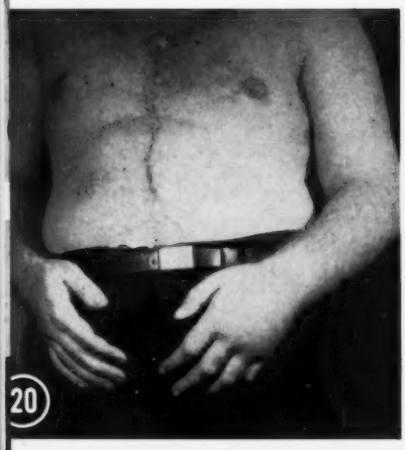




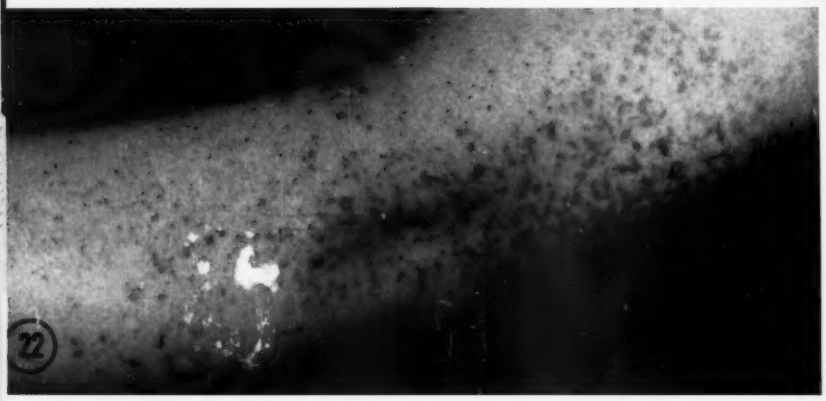


FIGURE 18. Enlarged nodes compressing the common bile duct. Clinical picture was characterized by jaundice.

FIGURE 19. Aorta surrounded and compressed by massive nodes due to Hodgkin's disease.

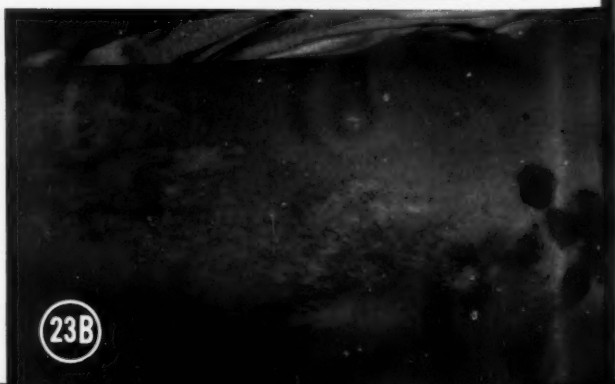
FIGURE 20. Edema of left upper extremity due to lymph channel obstruction.

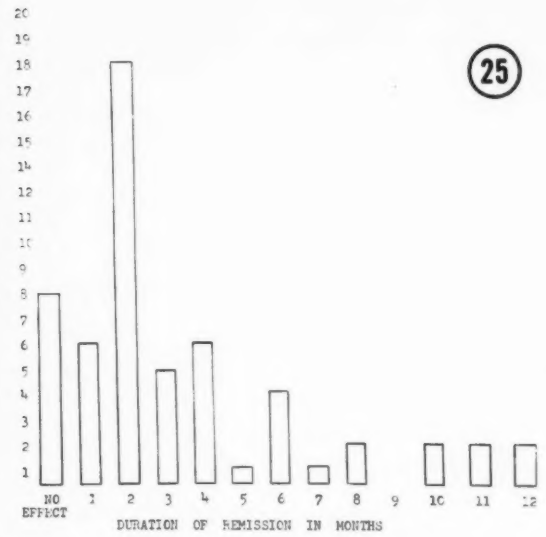
FIGURE 21. Marked lymphedema of the left breast.

FIGURE 22. Purpura complicating Hodgkin's disease.

FIGURE 23a. Herpes zoster represents one of the complications of Hodgkin's disease.

FIGURE 23b. A severe case of herpes zoster in Hodgkin's disease which has left extensive scar formation.





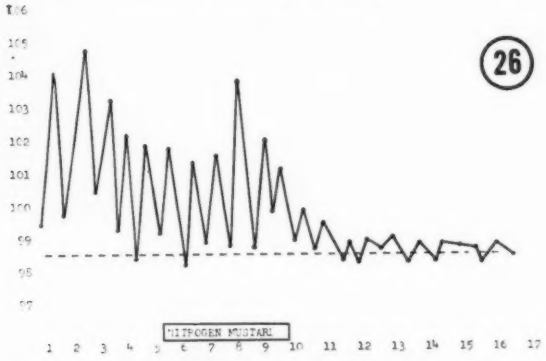


FIGURE 24. Massive enlargement of nodes in upper abdomen which caused marked abdominal swelling.

FIGURE 25. Duration of remissions in 57 patients with Hodgkin's disease treated with nitrogen mustard.

FIGURE 26. Typical effect on fever of nitrogen mustard.

FIGURE 27. Subsidence of pruritus and improvement of skin following nitrogen mustard therapy.

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FIGURE 28a. Skin before My-B-Den therapy.

FIGURE 28b. Skin after My-B-Den therapy.

The spinal cord becomes involved in about two per cent of Hodgkin's cases. Malnutrition and emaciation are complications late in Hodgkin's disease.

Now I should like very briefly to discuss therapy. Since 1904, x-ray therapy has been the standard treatment, and in my opinion it is still the best therapy, in selected cases. It is most effective in localized forms of Hodgkin's disease. But in instances of generalized adenopathy, and for patients who have had a recession not associated with any demonstrable pathology, nitrogen mustard is the therapy of choice. Over the past three years we have treated some 105 patients with 200 courses of therapy. The results have been rather remarkable, but they are also

disappointing in that nitrogen mustard does not cure. This chart in Figure 25 shows the number of remissions and their duration.

The greater number of patients to whom nitrogen mustard has been given have had remissions lasting approximately two months; a few have had remissions of a year or more. When a relapse occurs following the first administration of nitrogen mustard, the mustard can be given again and again. Over a period of three years we have given some patients as many as seven or eight courses before they finally became refractory to it.

Figure 26 illustrates what nitrogen mustard can do in some cases. This patient with Hodgkin's disease came into the hospital with a high temperature, an enlarged mediastinum, and one small node in the neck. Diagnosis was established. Nitrogen mustard was given at this point, and soon after the course was finished the temperature came right down to normal and the patient was normal for almost a year.

For a patient with pruritus (Figure 27), a course of nitrogen mustard caused the pruritus to disappear and the skin to become smoother. Thus nitrogen mustard not only effects relapses but has an effect on the associated symptoms. It will control pain, it revives the appetite, causes weight increase, and a return of strength which enables the individual to follow a normal way of living once more.

In the course of our experimental studies we had a most interesting experience. The patient involved had suffered for years from severe pruritus, which we were able to control with nitrogen mustard. Then came a time when even the nitrogen mustard was ineffective, and the severity of the symptom can be appreciated from the appearance of the skin (Figure 28a).

At this time I was experimenting with an adenylic acid compound known as "My-B-Den." I thought it might possibly improve the vitality and strength of the individual. Very curiously, the only two patients who happened to have pruritus reported that the symptom had disappeared after several days' medication. This is what happened to the individual above referred to after a course of "My-B-Den" (Figure 28b). You can see the marked healing of the lesions. Subsequent work has shown that about 50 per cent of patients with Hodgkin's disease pruritus respond to this substance. Unfortunately there still remains a large group who are not benefited, but the drug should be given a trial.

AUREOMYCIN APPEARS EFFECTIVE IN TREATING INFECTIOUS MONONUCLEOSIS

Aureomycin appears to be of definite benefit in the therapy of infectious mononucleosis, according to a preliminary study reported to the New York Academy of Medicine by Drs. Harold A. Lyons and Edward M. Hard of the U. S. Naval Hospital, St. Albans, New York. The investigators state, that although their data are "limited for so protean a disease as infectious mononucleosis, Aureomycin can be concluded to be effective in decreasing duration of fever, hospital stay, and total course of the disease by clinical measures." Lyons and Hard also feel that the duration of liver involvement is definitely reduced by Aureomycin therapy.

Diagnostic Clinic

Diagnosis and Treatment of Pulmonary Suppuration

EVARTS A. GRAHAM*
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THIS patient, a young man 22 years of age, was first seen by Dr. Norris in January, 1944. He has had a productive cough since the age of 6 following what was said to have been pneumonia. He has had four rather severe episodes of hemoptysis and intermittent blood streaking. He has a great deal of wheezing, occasional night sweats, and was underweight when he was first seen in 1944. Since then, however, he has gained 50 pounds and that is significant in what is going to follow.

At the age of 6 he had a tonsillectomy and adenoidectomy for persistent cough. He had pneumonia or pleurisy several times each winter until he was 17 years of age. He had nasal polyps removed on several occasions.

That story is typical, of course, of a chronic pulmonary suppuration. It practically always means bronchiectasis. We shall see if it means that in this case. Also, we expect that anyone who has had pulmonary suppuration for fifteen years or so is likely to be a little cyanotic, perhaps, is likely to have some bad odor to his breath, and is particularly likely to have some clubbing of his fingers and maybe of his toes. None of those features is present in this young man, probably because of the excellent treatment he has had during the last five years.

When I ask him about his present state of health he tells me that he works every day, full time. He is a maker of electrical surgical instruments. He has only a very slight suggestion of clubbing of his fingers and he is not cyanotic.

When I ask him, however, whether he gets short of breath more than the average individual he says that he does; he notices it especially when he runs for a streetcar or a bus or something of that sort. This, however, is not crippling. He says that he engages a little in athletics; he tries to play ball a little.

He looks to be in pretty good shape, not like a patient with any serious illness. He does have trouble, however, in the winters. Every winter he has several episodes of bad colds.

His bronchograms show a very characteristic finding in severe bronchiectasis. For example, there is marked saccular bronchiectasis of the right lower lobe and also in the middle lobe and possibly some in the anterior division of the upper lobe. There is a similar condition in the left lower lobe but also with evidence of definite atelectasis. The lingula is involved as well.

It is impossible to tell anything about the distribution of bronchiectasis or, at least, to tell enough about it merely from anteroposterior views. It is essential that lateral or oblique views be made also.

In the lateral view can be seen the very marked distribution of the bronchiectasis in the middle lobe and the right lower lobe. Apparently the disease is not confined to just one or two segments but involves practically all of those two lobes.

The films were made in 1944 and none have been made since, but there might not be any very marked difference.

When one has a disease of the respiratory tract of an inflammatory nature, usually the whole respiratory tract is more or less involved. That is a very important thing to remember. It is not confined merely to the upper or lower part. Therefore, when we are dealing with a condition of bronchiectasis, especially a bad one which has been present for a long time, we almost invariably find evidence of involvement of some of the nasal sinuses. The most commonly in-

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volved ones are the maxillary antrums. In addition, a more or less diffuse bronchitis is present which may persist for a few weeks even after the bronchiectatic part of the lung has been removed.

An x-ray film, also made in 1944, shows marked clouding of the maxillary sinuses, undoubtedly due to the presence of a thick membrane which probably occupies a large part of those sinuses. This condition gives symptoms to the patient. He will have to blow his nose much more often than the normal individual, and muco-pus will drip into his nasopharynx. These symptoms will continue as long as the marked thickening of the membrane of the sinuses is present.

We are dealing here, therefore, with a common condition of advanced chronic bronchiectasis plus advanced chronic infection of the nasal sinuses. If we think about the treatment for this man we must think also, therefore, in terms of upper respiratory tract involvement as well as lower respiratory tract involvement.

Presumably, because of the extent of the disease in this case, he has been treated conservatively. He has been instructed about how to carry out postural drainage. That means, of course, to lower his trunk so that gravity will help the secretions come out more easily, and he has had periodic bronchoscopic aspirations about once every three or four weeks. He had one just this morning. Also, he has had treatment with the new drugs, the new antibiotics, both by inhalation and parenterally, and with all of these things he has improved greatly. As I said, he has gained 50 pounds and is able to work on a full-time basis.

He is 22 years old. The question, of course, that comes up in regard to this patient, as with so many others like him, is: What will his condition be when he is 42 years old, that is, twenty years from now? Will he be able to work then? That question is always extremely difficult to answer. There is plenty of evidence, however, to indicate that once a severe bronchiectasis has developed it will never disappear on its own. The only procedure or method of treatment which will make it disappear is surgical eradication. There is no possibility with any drug yet discovered of sterilizing a case like this one to the extent that spontaneous healing will occur.

One does see occasionally examples of what might be called bronchiectasis, cases at least in which there is a dilatation of the bronchi seen

EVARTS A. GRAHAM

with lipiodol instillation, in patients who have practically no symptoms. In such patients, however, usually the dilatation of the bronchi is comparatively slight. Also, nearly always even in those patients there are periods in which there may be rather copious secretions.

I forgot to say that this boy says he thinks he brings up even now, when he feels comparatively well, about a teacupful of purulent sputum a day. During the winter he will have three or four severe colds, and during those times he will bring up much larger quantities of sputum than he does now.

There is considerable evidence that bronchiectasis is a progressive disease, although usually slowly progressive. It is possible, however, with the very effective antibiotic drugs which we now have, that these cases of bronchiectasis might be prevented from becoming worse as time goes on. No one can answer that question today. We shall have to wait for ten years perhaps to be able to answer it satisfactorily.

THE problem in this particular boy is, of course, whether he is a candidate for surgical treatment of his bronchiectasis. Is his dis-

ease too extensive for surgical treatment? Can't he get along well enough with conservative treatment to make it possible for him to be fairly comfortable and make a living and live for a reasonable number of years longer? Again, that is a difficult question to answer. I will say, however, that experience shows that if we take out the worst part of the bronchiectasis in a patient there is generally very marked improvement, even if some of the bronchiectasis is still allowed to remain.

In this case, he has a very definite atelectasis of his left lower lobe, along with very marked cylindrical bronchiectasis in it. Atelectasis of a chronic nature is always a serious disease; it always represents either a portion of lung which has become hopelessly impaired as a result of disease or a condition which is going to become infected sooner or later unless the atelectasis clears up.

The probabilities are very strong that his left lower lobe is not functional at the present time; it does not help him any in oxygenating his blood, and it is never going to be any good. We can say that with practically 100 per cent of certainty. Would it not be well, therefore, to remove the left lower lobe and at the same time perhaps remove the lingula of the upper lobe which corresponds to the middle lobe on the right side?

That brings up the question: How much lung tissue can be removed without leaving the patient a respiratory cripple? I can answer that question by saying that in children at least it is possible to remove everything except the two upper lobes and have these children develop in a comparatively normal manner; that is to say, to a degree which permits them to engage in athletic sports which are not too active, to go on and grow to their normal height, and to develop into normal individuals. In my own experience I have had about half a dozen children in whom such a procedure has been carried out, not all at once, of course, but gradually.

One questions, therefore, whether or not such a procedure might not be carried out in this man in several stages, perhaps in only two stages, perhaps in more than two. He is a little old for it, and that brings up the point that the best time to treat bronchiectasis is in childhood. The reason for that is that children go through the operation with surprisingly little difficulty and make generally surprising recoveries; their lungs fully compensate for the part of the lung which has been removed, and they develop into perfectly normal individuals.

We have recently made a study in St. Louis of 6 children who had a whole lung removed eight or more years ago while they were little children. We have made a study of respiratory functions dealing with the spirometric studies, the oxygenation of their arterial blood, and so on, as well as ordinary clinical studies, to see how well they have developed. These children without exception have developed into practically normal persons with almost normal respiratory functions. One of them, a girl, is a professional gymnast; another one, a man, is a mining engineer who works frequently at high altitudes and has never had any difficulty whatever so far as his respiration is concerned. I mention that because it is highly desirable to operate on people with bronchiectasis during their childhood rather than to wait until later. The older they get the more likely they are to have less satisfactory results from an operation. If, therefore, this young man waits twenty years longer and then comes around, more or less a respiratory cripple because his lung has been constantly bombarded with infection during all this time, he will have developed perhaps a rather high degree of emphysema, and then it will be too late to accomplish much by surgery.

In my own opinion it would be well for this patient to have an operation on his left side at this time to remove his left lower lobe, which is doing him no good anyway, and at the same time to remove the lingula; then wait a year or maybe two years to see how much benefit he gets from this procedure, also to get a little better impression of whether he is likely to be a respiratory cripple if a similar operation is carried out on the right side. Also, because this is a disease of his whole respiratory tract and because he has this marked chronic infection of his nasal sinuses, it seems to me it would be wise to have a radical operation on his maxillary antrums. There is nothing gained by merely punching little holes in them. Such a procedure accomplishes something only for a matter of a few weeks and then the patient is just as bad as before. What is needed in these cases is removal of this membrane by the operation known as the Caldwell-Luc operation, which is easily performed and generally gives very satisfactory results.

Before undertaking any operation on this man for the removal of any portion of his lung, he should be studied more carefully by means of modern tests of respiratory function. I see a note here on the history that those are about to be done, but we do not have any record of them now. We sometimes find that the patient is much more crippled in a respiratory sense than we have any idea.

What about operation? What about the results? Twenty-five years ago this operation was much dreaded because of the high mortality associated with it—that is, the operation of lobectomy, one or two lobes, as the case may be. Nowadays, that is no longer true. Some of you perhaps will be unwilling to believe me when I say that the mortality now, in the hands of thoracic surgeons who know their business, in lobectomy for bronchiectasis is scarcely over 1 per cent.

In our experience in the last 250 cases of lobectomy performed for bronchiectasis the operative mortality has been 1.2 per cent, so it has ceased to be a dangerous operation when properly safeguarded by all the modern methods of anesthesia, blood transfusion, antibiotics, and so on. Furthermore, whereas twenty-five years ago the patient had to expect to stay in the hospital anywhere from a month to three or four months after operation, now we expect patients who have had lobectomies for bronchiectasis to leave the hospital in from eight days to two weeks, practically never more than two weeks. It has therefore become an operation not accompanied by great danger or by long periods of convalescence. On the other hand, we do not want to let the fact that the mortality is so low lead us on into operating where operation should not be performed; that is to say, we certainly do not wish to leave the patient a respiratory cripple from having had too much lung tissue removed. That is very bad.

Another improvement which has occurred in the surgical management of bronchiectasis is that it may be necessary to remove only one or two segments of a lobe instead of the whole lobe if the bronchograms show only a limited involvement.

Of course, in a limited length of time it is impossible to discuss this question adequately. There is one other type of bronchiectasis which I should like to mention, however, and that is bronchiectasis confined to the upper lobes. That type of bronchiectasis practically always is due to tuberculosis. It is a totally different disease from the ordinary bronchiectasis which we see involving the lower lobe, the right middle lobe, or the lingula of the left lobe respectively. That type of disease is best treated, as a rule, also by removal of the infected lobe, because a patient with tuberculous bronchiectasis involving, we will say, the left upper lobe, casts off large numbers of tubercle bacilli in his sputum as a rule. He is therefore a menace to his family and to his community, and the only way of getting rid of that disease is by removing it just as we remove ordinary pyogenic bronchiectasis in a lower lobe.

A year or two ago I spoke to this Association about a complication of bronchiectasis which is an interesting one—one which is confined to the middle lobe of the right lung.[1] This is due to an interesting disturbance chiefly of the lymph glands which are deposited along the middle lobe bronchus. Swelling of these lymph glands results in the production of edema of the bronchus underneath, which in turn becomes more easily compressible because of its softening; the bronchus becomes occluded, and that portion of the lung becomes atelectatic and therefore subject to infection. These patients present themselves generally with chronic infection of the right middle lobe, often with bronchiectasis in it, and the only satisfactory method of curing them is to remove the lobe.

There is still one other feature of chronic pulmonary suppuration which should be mentioned, and that is the association of chronic pulmonary suppuration with bronchiogenic carcinoma. This is something of the greatest importance. Simply because a state of chronic suppuration is diagnosed, one shouldn't dismiss the possibility that maybe there is something more serious than that also present, namely, a carcinoma. Anything that obstructs the bronchus is going to cause infection in the obstructed part of the lobe. Since a carcinoma is one of those agents which frequently obstructs the bronchus, we always expect some degree of suppuration in the obstructed lobe if the obstruction has gone on for a long enough period of time.

[1]Graham, E. A., Burford, T. H., and Mayer, J. H.: Middle lobe syndrome. Postgrad. Med. 4:29-34 (July) 1948.

Diagnostic Clinic

The Cerebral Palsy Problem

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CHILDREN'S REHABILITATION INSTITUTE, BALTIMORE

I AM going to discuss only certain phases of the cerebral palsy problem, because the whole subject is so broad that it is impossible to cover every aspect in a limited time. I think some of the most interesting features of the condition, especially to a group of professional men, are the studies of the etiology.

It was formerly supposed that cerebral palsy was caused entirely by injuries at the time of birth, but this theory has long since been found to be false.

The statement was made around 1920 that cerebral palsy was chiefly the fault of the obstetricians, and they took a good deal of punishment in various papers presented at that time. Since then, however, it has been found on statistical study that only a very small percentage of these cases could in any way be attributed to actual bad obstetric technic.

DEVELOPMENTAL DEFECTS

The large majority of them appear to be due to developmental defects in the child. We do not, of course, know the cause of these defects. The amount of interest that has been given to children who had blindness with cataracts resulting from the mother's having had German measles during the first three months of pregnancy has made it interesting to follow this up with regard to what other conditions may cause defects in the child during the first three months of pregnancy.

We often hear of mothers who are debilitated or very sick during that period of time and who have various types of diseases and illnesses, but there has never been any correlation with regard to this. However, statistics are becoming more and more striking concerning the fact that something happening in that early period of pregnancy may result in abnormalities in the child.

In the child in whom we suspect that this condition may occur we do sometimes find cerebral palsy associated with the congenital cataracts that one sees with a history of German measles in the mother. We also find a certain group of congenital anomalies or abnormalities which include such conditions as cleft palate, hairlip, and spina bifida. This developmental factor also frequently seems to be associated with midline defects in, for example, the cerebellum, resulting in an ataxia in the child.

There is a whole group of these midline defective developmental conditions, and they are not all alike. For instance, in the child who has a cerebral palsy which is entirely symmetrical, we usually find a very high roof of the mouth so that closure of the hard palate is complete and there is not a cleft palate but almost a cleft palate. That particular finding is constant in a good many of these children who show a rigidity of about equal distribution on both sides of the body. Obviously, such a condition could not result from an injury at the time of birth, because the high roof palate could be noticed at birth and must, therefore, have preceded birth by a number of months. So there is a whole

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group of these children, most of whom fall in the subclassification of cerebral palsy of the rigidities, who have this particular picture of developmental defects.

Some of these children are definitely microcephalic, and others are not. Therefore, we have that large group of cases of cerebral palsy to think of which result probably from very early difficulties of development.

RH FACTOR

In breaking down the statistics we find a certain type of athetoid child who possesses certain associated characteristics the nature of which is not quite clear. The athetoid child, of course, is characterized by the presence of involuntary motions, purposeless moving of the arms, legs, and sometimes the face.

It has been observed that there are a number of different kinds of athetosis, each having a few specific features that make it into a definite syndrome. First we see the purposeless motions; then we examine the eyes and find that there is difficulty with the upward and downward motions, but that the lateral motions are perfectly normal. The significance of difficulty with the upward and downward motions of the eyes is not known as yet. Then as this child gets a little older it is found that he has a definite hearing defect—he is not completely deaf but his hearing is impaired in the upper pitch range, with practically normal hearing in the lower pitch range. This picture, then, becomes a rather typical one of athetoid difficulties and difficulties of eye motions and hearing.

We were able to identify this picture about ten years ago, but did not have any idea as to its cause. When studies were made in the last few years with regard to the Rh factor, on looking back through the records, it was found that this particular type of athetoid patient had a history of jaundice at birth in every single case. Since then, in as many of those patients as possible, we have had the mother and child tested for the Rh factor, and we found that all of them had Rh factor difficulties, that is, the mother was negative and the child was positive. So there has come out a very definite etiologic factor in a certain type of cerebral palsy, the athetoid type, when it is associated with a hearing loss.

Many athetoid children that we see now have had multiple or complete transfusions, yet they still present this athetoid picture. Naturally, only the ones that present this picture would be seen by me or others working in this field, so that the question of whether multiple transfusions will relieve the situation cannot be stated from the cases that we see, since they are obviously selected.

It would be interesting to find out from pediatricians in general how many of these Rh positive children who have had transfusions do not have any resultant damage. The number of cases of cerebral palsy that result from the Rh factor difficulty is not very great in the total field of cerebral palsy, because, of course, the Rh factor difficulties are not very common in the population at large. This, then, is another etiologic factor for cerebral palsy which obviously has nothing to do with injury at birth.

ANOXIA

Schreiber in Detroit described cerebral palsy resulting from the use of the twilight sleep type of drugs in the conduct of labor. It has been found that in the use of these drugs, which are respiratory depressants, there is naturally a depression of the child's respiratory function and a resultant late breathing, with the necessity for an oxygen tent. In many of these cases we find damage to the brain from lack of oxygen, a cerebral anoxia. This, of course, is not true where such anesthetic agents as ether and others which are respiratory stimulants are used, because obviously they would have no effect on the child's respiration. This might, in the broad sense, be called a birth injury.

PREMATURITY

Another mechanism of the production of cerebral palsy which is quite interesting is associated with prematurity. When a child is premature he is naturally small and frequently is born very rapidly. The sudden drop from intrauterine pressure to air pressure is too great a change for the walls of the blood vessels to withstand. These walls, of course, are not as strong in the premature infant as they would be if the child were born at full term. Therefore, from this change in pressure a hemorrhage results, and the only place in which the hemorrhage can cause damage is directly beneath the anterior fontanel; this is the only expansible part of the brain at that time, the rest of it being

WINTHROP M. PHELPS

covered with the skull. The underlying part of the brain beneath the anterior fontanel is the area for the legs, the pre-Rolandic area.

The child with cerebral palsy resulting from this kind of damage has a spastic paraplegia, usually involving the legs only. The arms escape, and speech and mentality are normal. This type of damage is so consistent with a history of premature, rapid birth that very frequently you can almost tell what the history of that birth was by the type of cerebral palsy present.

THERE are many other places in the brain and spinal cord from which spastic paraplegia can result. Obviously, damage anywhere through the pyramidal system, in the leg area, in the high cervical region, and in the cord can result in a paraplegia. The differential diagnosis must be made carefully to be sure that the condition is of cerebral origin. Distinguishing it from the cord type is not difficult because the sensory control is not involved and there is no loss of sphincter control in the cerebral type.

We have discussed congenital defective development, the Rh factor, anoxia from lack of oxygen at birth, and prematurity as four causes of cerebral palsy which are not in any way directly associated with the obstetric history.

BIRTH INJURIES

Next we come, chronologically, to the true birth injuries. The first of these would be injuries from the application of forceps; these are not too common, but occasionally result. Usually the type of child seen with such an injury is the hemiplegic with involvement of only one side of the body. The effect of pressure of the forceps on both sides resulting in multiple fractures of the skull would probably be severe enough that in most cases the child would not survive. However, when one blade of the forceps presses on one side of the head and the other side escapes, with perhaps a minor fracture of the skull or a slight depression with a subdural hemorrhage, hemiplegia results.

There is also the type of cerebral palsy which results from stretching of the neck during birth. This is most commonly seen in breech presentations where there is difficulty in delivering the aftercoming head, but it also occurs when there is difficulty in disengaging a shoulder of the child from behind the pubis, when excessive traction is made on the neck. This traction results in a stretching of the neck, a pulling down on the tentorium, and a consequent rupture of the vein of Galen which lies in the tentorium. The hemorrhage from this rupture involves the basal ganglia, so that we have in this type of birth injury a still different kind of cerebral palsy—athetosis from basal ganglia damage but a totally different type of athetosis from that seen in cases of Rh factor athetosis. This type of athetosis is characterized by excessive tension, very rigid muscles, usually very strongly developed with constant contractions, and is described as tension athetosis.

Subclassification of athetoids has been made so that there are twelve different identifiable types, and we do not know the causative factors in a good many of these as yet.

POSTNATAL INJURIES

The next period at which cerebral palsy can occur would be after birth, and we find that sometimes there will be severe convulsions during the first two or three weeks of life from either a high temperature or some digestive

disturbance in a previously normal child. The severity of convulsions at this age is enough to bring about a brain hemorrhage. Thus we have a postconvulsive type of cerebral palsy from convulsions during the early weeks of life.

Then there is a group which results from children having whooping cough under three months of age. The characteristics of the cerebral palsy in this group are more of a rupture of a brain vessel, probably from the violence of the paroxysm of coughing, than an encephalitis from the whooping cough virus. We have a very identifiable type with a localized lesion, usually a hemiplegia.

Next is the group of postencephalitic virus conditions, usually following any of the exanthemata, such as cerebral palsy resulting from a postmeasles encephalitis, a postpertussis encephalitis, or almost any other of the children's diseases. This type of cerebral palsy is more characteristic of paralysis agitans juvenilis or infantile Parkinson's disease.

Another and increasing cause of cerebral palsy is a violent accident resulting in head injuries. These accidents increased tremendously when automobiles began to be driven rapidly.

Cerebral palsy can, therefore, be caused by a large variety of etiologic factors, and these factors go back to the first months of pregnancy and continue throughout the child's intrauterine life and birth and through the rest of his life. Various types of palsies result; they are not all alike.

It seems very important to point out that we still do not know the exact position of the brain damage in many of the children. The neurologic textbooks describe many well-recognized syndromes resulting from brain tumors or brain injuries in previously normal people. These syndromes cannot be identified in the same way in the child who has brain damage at or before birth. When a syndrome of a certain part of the brain is identified in an adult who had a previously normal motor system and nervous system, all the functions of the other parts of the brain have been fully developed and only one portion is injured. It is very different if this same portion of the brain is injured *before* the other parts of the brain have had a chance to develop their function, so that the syndrome as described for an acute condition like a brain tumor or brain injury would not resemble at all the syndrome of brain injury or disturbance at or before birth.

It is very important to try to identify each type of cerebral palsy very exactly and to have an exact description as to whether the patient is a spastic, athetoid, rigidity, ataxia, or a tremor type, so that if these cases should come to autopsy we could learn more about localization of various defects or injuries to the brain.

Such a project of studying these carefully identified brain lesions is being carried out by the American Academy on Cerebral Palsy; headquarters for these studies is in Chicago at the present time. The project is a new one and there have been no reports as yet of the results obtained, but it is a very important project.

I think that from what I have said you can see that we can almost completely clear the obstetrician of any great blame in the cause of cerebral palsy. The few birth injuries that we do know to be the result of obstetric trauma are in most cases unavoidable, and it is interesting to note that the number of cases of cerebral palsy in the population seems to be constant. If a survey is made of the number of cases seen in the mountains and very isolated mining districts where the children are often born without obstetric help, and this is compared with the number of children with cerebral palsy in an advanced obstetric hospital in a large city, it is found that the actual percentage of cases of cerebral palsy is just about the same.

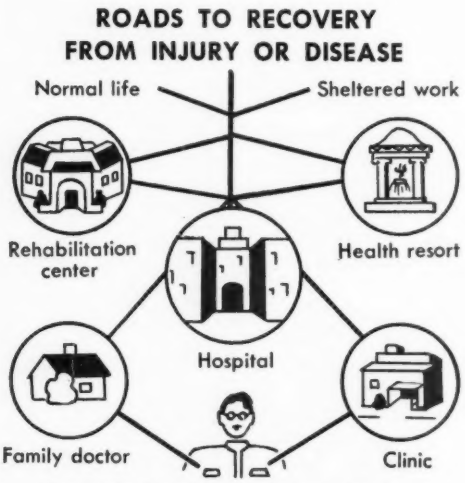
Scientific Exhibit

Spa Therapy

F. A. HELLEBRANDT, M. D. AND SARA JANE HOUTZ, M. S.

MEDICAL COLLEGE OF VIRGINIA, RICHMOND

WATER has been called the "Universal Panacea." It stands among the most ancient of all remedial agents. Its use for healing purposes is recorded in the whole of the written history of mankind. No other agent is capable of producing so great a variety of physiologic effects!



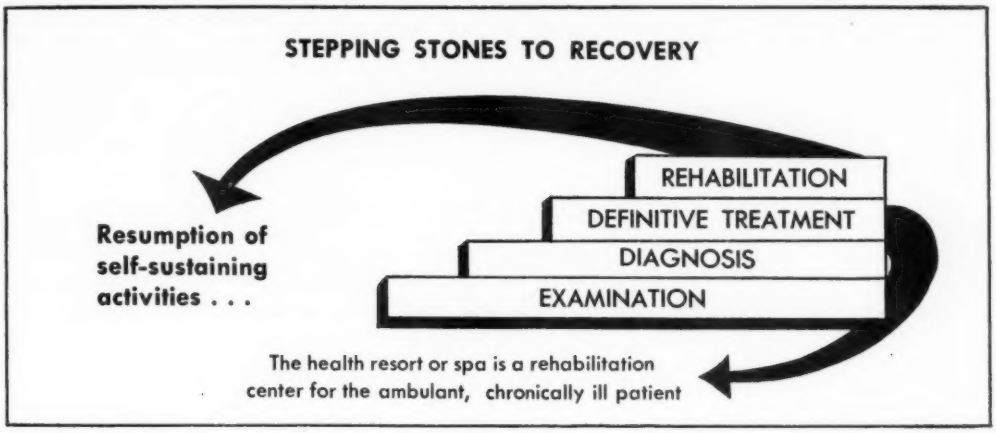
Illustrating the place of the spa facility in the physician's armamentarium

DEFINITION OF A HEALTH RESORT

An institution which gives major attention to use of climatic and other natural therapeutic resources including mineral waters and peloids with which it is endowed by reason of its location. While the therapeutic use of the natural resources is the purpose of the institution, other remedies may be applied or administered as indicated.

The Committee on American Health Resorts of the Council on Physical Medicine of the American Medical Association assists the physician by listing climatic and mineral spring facilities believed to have value in the treatment of the sick and disabled. To be accepted for listing, a health resort shall: be located where natural healing agents or special climatic conditions are found, be operated under adequate medical

Adapted from the exhibit symposium on Physical Medicine and Rehabilitation sponsored by the Baruch Center of Physical Medicine. Prepared with the cooperation of Walter S. McClellan, M.D., Chairman of the Committee on American Health Resorts, and Howard A. Carter, Secretary. Council on Physical Medicine and Rehabilitation, American Medical Association.


STEPPING STONES TO RECOVERY
REHABILITATION
DEFINITIVE TREATMENT
DIAGNOSIS
EXAMINATION
Resumption of self-sustaining activities . . .
The health resort or spa is a rehabilitation center for the ambulant, chronically ill patient

supervision, have a physical plant suitable to administer treatment with the natural agents, and have available accessory forms of physical medicine under proper supervision.

Components of health resort or spa therapy include: freedom from stress; rest and relaxation; diversional and recreational activities; graded exercise, "terrain cure"; dietary control; mineral waters and peloids; climatic factors and other physical agents.

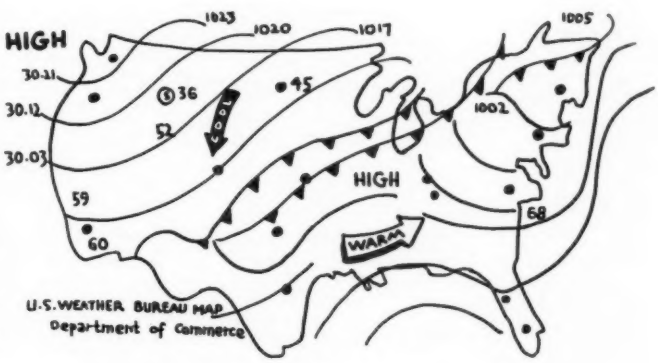
The temperature and chemical constituents of mineral waters depend on the geological formations and strata through which waters flow and the depth from which they rise. Natural springs vary as to temperature, mineral constituents, gases and radioactive material. Their physiochemical properties determine their therapeutic use.

Pelotherapy is the treatment of disease by means of mud baths or packs. Their plasticity enables them to be applied readily to any part of the body. The specific heat of peloids is much lower than that of water. Temperatures up to 50° C. are tolerated. Owing to their poor conductivity, peloids cool very slowly. Thus peloids provide an excellent medium for conduction heating.

Frequently health resorts have available accessory forms of physical medicine, such as therapeutic pool, Hubbard tank, whirlpool bath, massage, electrotherapy, muscle training and rehabilitation exercise.

CLIMATIC FACTORS

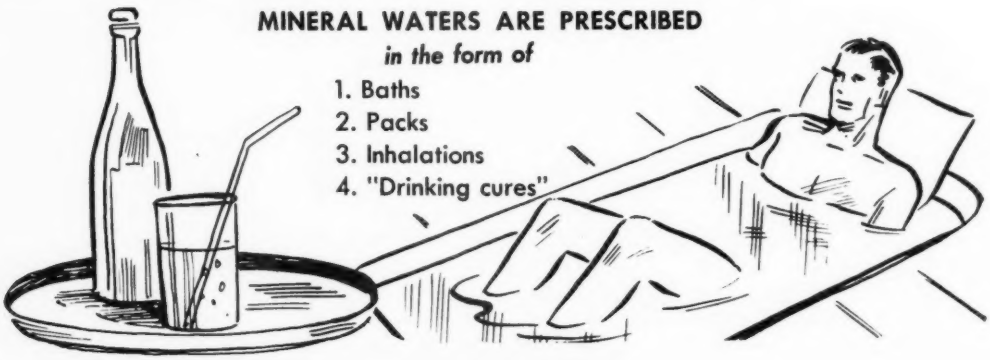
Altitude — Fresh Air — Sunshine

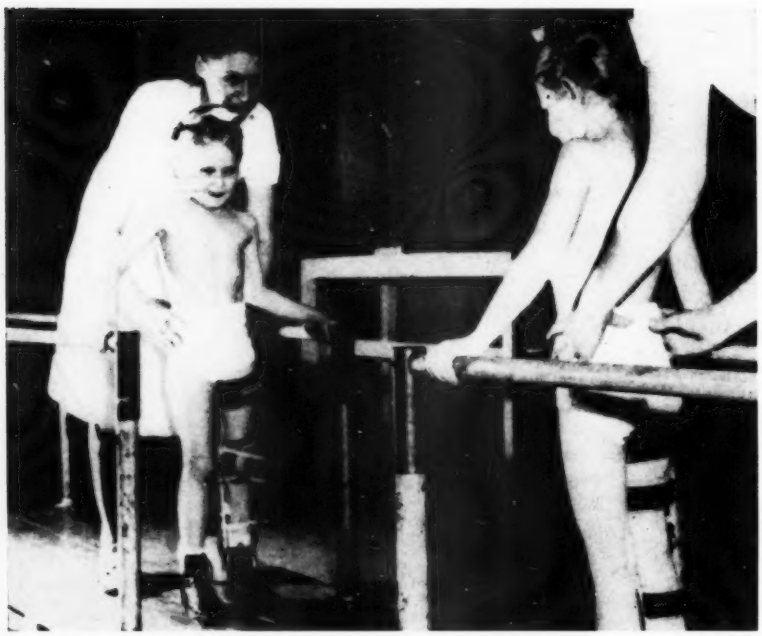


Temperature — Wind — Barometric Pressure — Humidity

Frequently health resorts have available accessory forms of physical medicine under proper supervision.

MASSAGE





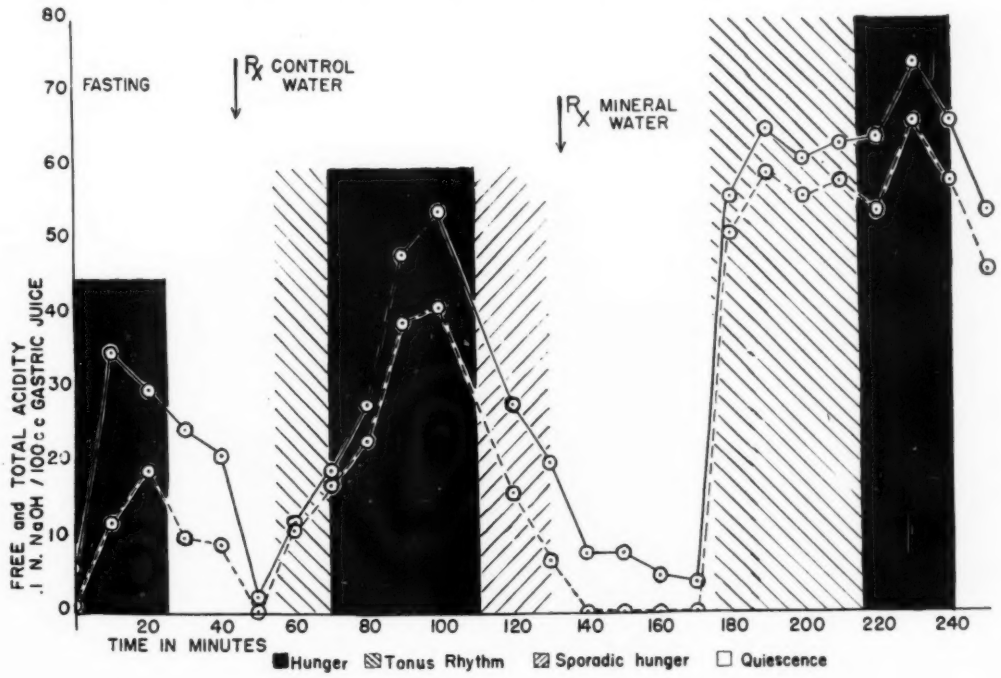
REHABILITATION EXERCISE

SIMON BARUCH'S advice to his professional brethren . . . Uttered at a time when hydropathic charlatanism was rampant on the European continent:

"The study and judicious application of hydrotherapy in regular practice will accomplish more for the protection of the people against the quacks than prosecutions through legal channels. The patient cares little *how* he is healed; he certainly prefers to be cured by the empiric to being kept in continuous pilgrimage to the scientific doctor's office. A correct diagnosis does not interest a sick man so intensely as correct treatment."

The Principles and Practice of Hydrotherapy

SIMULTANEOUS SECRETORY AND MOTOR OBSERVATIONS



THERAPEUTIC TEST

Originated by Simon Baruch.

No remedial agent merits the confidence of the physician unless it fulfills the following conditions:

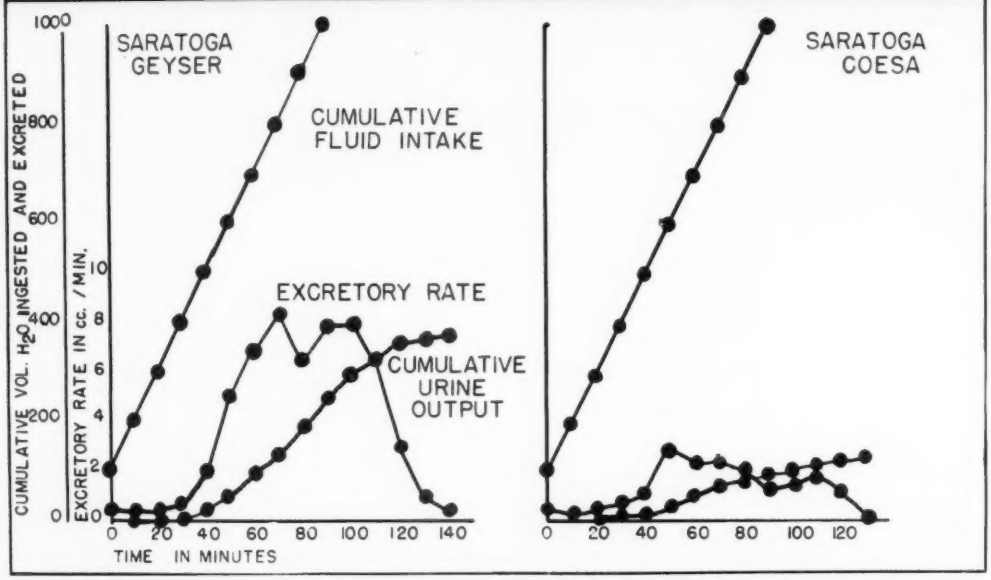
1. Ready accessibility
2. Rationale ascertained by experiments on a physiologic basis
3. Facility of dosage
4. Reliable clinical observations

MEDICAL HYDROLOGY

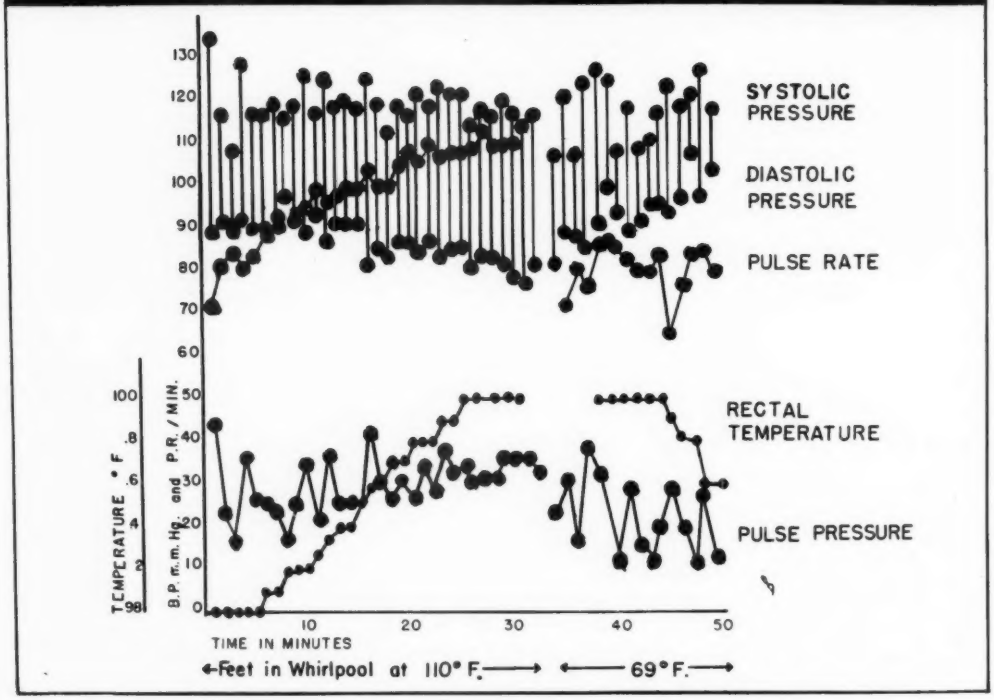
Baruch's concept of the two steps essential to the establishment of a science of medical hydrology:

1. Earnest and conscientious investigation of physiologic and clinical claims for hydrotherapy
2. Better instruction of medical students

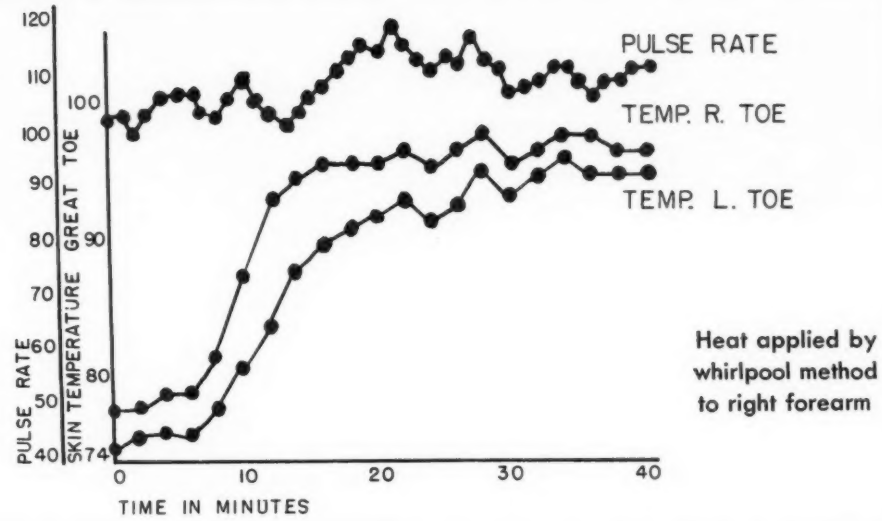
INFLUENCE OF SOME MINERAL WATERS ON EXCRETORY RATE OF KIDNEY



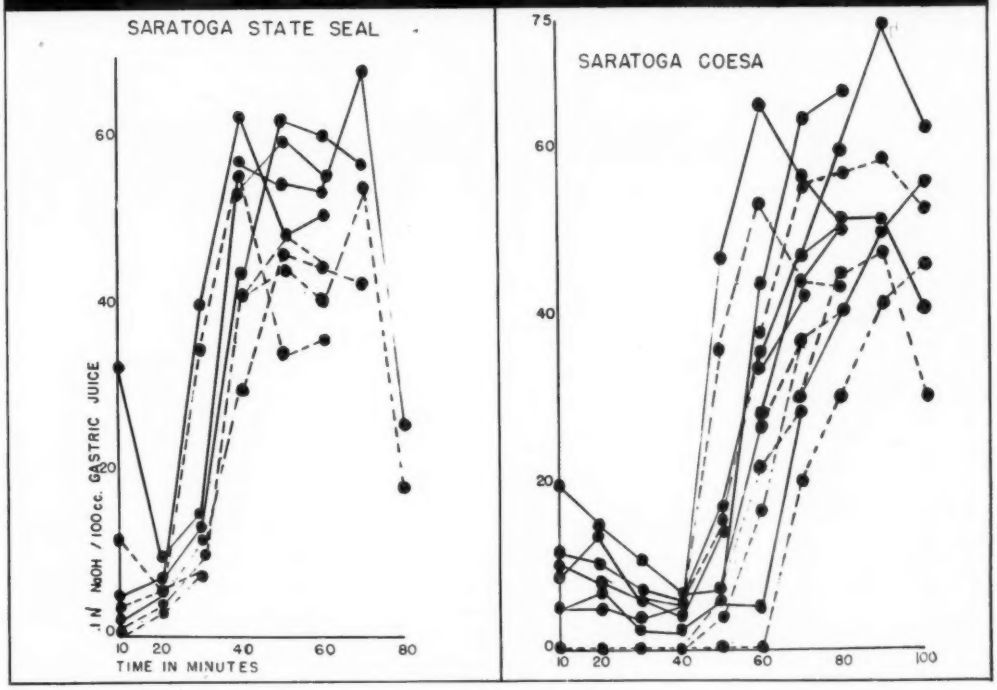
SYSTEMIC EFFECTS OF REGIONAL HEATING



REFLEX VASODILATATION DURING APPLICATION OF HEAT



CONSTANCY OF THE GASTRIC ACIDITY RESPONSE



GENERAL PRACTICE *Review*

To provide the general practitioner, as well as the specialist with concise, readily available information on the latest, proved methods of treatment of conditions commonly encountered in an average practice, POSTGRADUATE MEDICINE *offers this department to its readers. It is not, of course, intended to present these discussions as the only acceptable therapeutic procedures to be used, but rather to offer simple regimens and recommendations based on the extensive experience of the physicians who prepared these summaries.*

Clinical Differentiation of

Chronic Pyelo and Chronic Glomerulonephritis

ROBERT D. TAYLOR

RESEARCH DIVISION AND FRANK E. BUNTS EDUCATIONAL INSTITUTE, CLEVELAND CLINIC FOUNDATION, CLEVELAND, OHIO

PROTEINURIA, pyuria, hematuria, cylindruria, eventually hypertension and renal failure can result equally from chronic glomerulonephritis and chronic pyelonephritis. Since the time of Bright, glomerulonephritis has been widely studied and discussed, so that it is often the first diagnosis in patients showing signs of renal disease.

The incidence of glomerulonephritis is only 0.7 per cent[1] and is not nearly as great as that of pyelonephritis, which Raaschau in Copenhagen found in 5.6 per cent of 3,607 postmortems.[2] Glomerulonephritis is a relentlessly progressive disease; pyelonephritis is one that can be cured or controlled. Recognition of pyelonephritis is therefore of prime importance.

Glomerulonephritis is believed to be a continuing, destructive antigen-antibody reaction which takes place in the glomeruli while pyelonephritis is a focal or diffuse inflammatory process that follows infection. It can involve glomeruli, tubules, interstitial tissue, and even the arterioles, so that a proliferative endarteritis appears. The primary pathologic changes occur in the glomeruli in glomerulonephritis, but as the disease advances, tubules are damaged because of reduced blood supply, scarring, or obstruction caused by cast formation. Pyelonephritis produces damage first by the changes of inflammation and later because of scar formation and contraction.

The most common infectious organisms in pyelonephritis are the colon bacilli and streptococci. In some cases, the infection is secondary to anatomic lesions which prevent the free flow of urine. In this group, surgical correction of the obstruction usually permits ready correction of infection. In the remaining pyelonephritic patients, the infection is primary with no demonstrable anatomic abnormalities which might predispose to urinary stasis. It is this group that must be separated from those patients with glomerulonephritis. The tabulation given on page 217 is often helpful in this respect.

Glomerulonephritis can be treated only symptomatically. Pyelonephritis can often be cured or so controlled that renal failure and hypertension need not follow. Once the offending organism is culturally identified, treatment can be started with sulfadiazine. This drug is preferred because it is often effective against both coccal and bacillary organisms, and because it can be taken orally for long periods. Dosages sufficient to establish blood levels of 6 to 8 mg. per 100 cc. are needed at the outset. Four grams at once and a gram every four hours thereafter with equal parts of sodium bicarbonate usually suffice. A fluid intake of at least 300 cc. daily promotes good urinary drainage and inhibits crystal-formation in the urine.

Because renal excretory function may be depressed, untoward elevation of blood levels is pre-

	CHRONIC PYELONEPHRITIS	CHRONIC GLOMERULONEPHRITIS
	Clinical Findings	
HISTORY	More common among females; often follows marriage or pregnancy. Recent or remote history of chills and fever with dysuria. Nocturia is more frequent during active phase. Edema is rare except in terminal state.	There is no sex predominance. There is sometimes history of acute hemorrhagic glomerulonephritis. More often proteinuria is discovered during routine examination. Edema is frequent. Nocturia gradually increases and becomes continuous.
PHYSICAL FINDINGS	Patients may appear acutely or chronically ill. Blood pressure is usually normal and becomes elevated only as renal failure supervenes; occasionally acute hypertension. Costovertebral angle tenderness demonstrable. No edema. Fever is common and may be of septic type.	Unless process is very active or terminal, patients appear well. Blood pressure is often normal; commonly moderately elevated early in course; high in later phases. Dependent edema. Mucous membranes and skin appear moderately pale. Fever rare, due to intercurrent infection or massive edema.
	Laboratory Findings	
ADDIS TEST	Ability to concentrate urine is usually fairly well preserved.	Until advanced and terminal phases, concentrating power moderately depressed.
Tubular function	If it is depressed, the change is proportionate to decrease of glomerular filtration. Concentrating ability may improve with treatment.	It is not impaired in proportion to filtration rate. (Measured from urea clearance.)
Proteinuria	Usually not more than 1 to 2 gm. per twenty-four hours.	Usually above 2 gm. per twenty-four hours—commonly 4 to 10.
Cylindruria	May be excessive during active inflammation and wholly remit in intervals. Casts are usually granular or cellular (leukocytes).	Casts are constantly increased in number and until terminally are predominantly hyaline, or if cellular, show red cells and epithelium.
Hematuria	During active infection may be considerable. It clears with treatment.	Varies in degree but is almost constantly present.
Pyuria	May be great. Leukocytes show great cytoplasmic motion (vital stain or phase microscope).	Moderate. Leukocytes inert.
UREA CLEARANCE		
Filtration rate	Moderately depressed and in proportion to tubular damage.	Greatly depressed, more so than tubular function.
Blood urea	May be elevated to 50 to 60 mg. per 100 cc. in spite of adequate filtration because of fever-induced excess protein catabolism.	May be normal in spite of depressed clearance.
BLOOD		
Hemoglobin	Normal or depressed if disease is long-standing.	Early—normal. With appearance of azotemia—progressive anemia.
White cells	Often moderate leukocytosis.	Normal.
Proteins	Usually normal.	Albumin fraction often low.
URINE		
Culture	May at times be sterile, but the same organisms can usually be recovered with repeated cultures.	Sterile.
X-RAYS	In primary pyelonephritis kidney pelves, ureters, and bladder have normal shadows until late in the disease. There then may appear blunting of calyces and distortion of pelves. In secondary types an obstructive lesion is demonstrated by intravenous or retrograde pyelogram.	Normal.

vented by daily control of blood concentration during the early intensive therapy. As pyuria decreases and after forty-eight afebrile hours, the dosage is decreased to 0.25 or 0.5 gm. 4 times daily. These quantities provide urinary concentrations of 50 to 100 mg. per cc. and can be continued indefinitely, providing each tablet is taken with 2 full glasses of water. In most cases, it is good practice to prolong this program for six to eight weeks after all signs of infection have subsided.

At the start of the program, the sensitivities of the organism to sulfadiazine, streptomycin, penicillin, aureomycin, and chloromycetin should be determined. If the sulfonamide is not bacteriostatic *in vitro,* it can be replaced at once by a more effective agent. Especially in secondary pyelonephritis, once urine cultures have become sterile, it is well to maintain the small dosages of sulfadiazine in repeated courses.

These patients should be considered to have chronic ailments or at least as being vulnerable to reinfection with any subsequent illness, operation, or pregnancy. If they are apprised of the early signs of urinary tract infection and are told to seek treatment at the first suggestion of its return, much distress and kidney damage can be prevented.

If after the infection is controlled, signs of renal insufficiency and proteinuria persist, there are two forms of medication which have some value and may be administered for indefinite periods. The fish oils which contain vitamin A have been shown to have an unknown substance or substances which increase renal blood flow, filtration rate, and tubular excretory capacity.[3] We have given Alphalin (Lilly) which is a convenient source of these oils, 25,000 units 4 times daily and believe the well-being and possibly the longevity of the patients are enhanced.

Should the degree of proteinuria be great enough to cause excessive cast-formation, it is wise to maintain an alkaline *p*H of the urine since the precipitation of protein is less great in such a medium. This can be accomplished by giving potassium citrate, 1 to 2 gm. four times a day.

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Treatment of Cardiac Arrhythmias

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It is assumed that the diagnosis has been clearly established in each of the arrhythmias to be discussed and no discussion of diagnostic procedures will be undertaken. A consideration of etiologic factors will be necessary in order properly to classify and logically to treat these patients.

Premature beats may be benign and associated with nervous tension or toxic agents such as caffeine, nicotine, or alcohol. Sometimes they are associated with flatulence.

Premature beats are often seen with organic heart disease such as rheumatic or other types of infectious myocarditis, valvular lesions, coronary disease, and hypertension.

Premature beats may produce disturbing symptoms, or may occur without the patient's being aware of their presence.

Treatment depends on the etiologic factors and should be approached as follows:

Asymptomatic and no detectable etiologic factor—No treatment should be undertaken. Too much attention to benign asymptomatic arrhythmia may create a cardiac neurotic.

Symptomatic but without a demonstrable organic basis—(1) Eliminate all intoxicants and focal infection. (2) Correct digestive disorders. (3) Reassure and outline hygienic rules of living with a physical exercise program. (A physical training program does much to convince the patient that he does not have organic heart disease.) (4) Drugs:

Sedation.

Quinidine sulfate.

Digitalize if quinidine does not abolish the arrhythmia.

Potassium acetate 25 per cent aqueous solution 4 gm. every three to four hours by mouth.

Premature beats associated with organic heart disease require treatment of the underlying disease

plus the procedures discussed under the preceding classification.

Paroxysmal auricular tachycardia: Determine the existence of organic disease or aberrant conduction pathways such as exist in the Wolfe-Parkinson-White syndrome.

Vagal stimulation—Carotid sinus pressure; orbital pressure; induced emesis; breath holding.

Digitoxin 1.2 mg. or lanatosid C. 1.6 mg. intravenously as a single or divided dose. (Be sure the patient has not been previously digitalized.)

If above fails, give quinidine sulfate, 0.2 gm. trial dose. If no untoward reaction occurs give 0.2, 0.4, 0.5, 0.6 gm. at two-hour intervals until the arrhythmia has ceased; then 0.3 gm. every four hours for twenty-four to forty-eight hours.

Sedation is often helpful, especially in those who have never had a previous attack. Sodium luminal 2 to 5 gm. by hypodermic or even demerol or morphine may be indicated if the patient is greatly disturbed. In those with frequent recurring attacks opiates must not be used.

Other drugs sometimes used are:

Mecholyl 15 to 25 mg. by hypodermic (atropine to be used if untoward effects occur).

Prostigmine methyl sulfate 1 mg. injected intramuscularly.

Magnesium sulfate 20 per cent solution, 20 cc. slowly intravenously.

Paredrine 40 to 60 mg. three times a day by mouth.

Prostigmine bromide 15 mg. three times a day by mouth.

Direct electric stimulation of the vagus nerve with faradic current or injection of stellate ganglion has been used in intractable cases.

Intravenous procaine 2 per cent solution intravenously is often efficacious but may be dangerous and should be used only by one experienced in this type of therapy.

Auricular fibrillation and auricular flutter: When considering a therapeutic approach to these arrhythmias one must determine the associated etiologic factors, the duration, and whether or not the arrhythmia is paroxysmal.

The circus movement theory of Lewis has recently[1] given way to a concept that considers auricular fibrillation, auricular flutter, and paroxysmal auricular tachycardia as all being rhythms arising from an ectopic focus. They differ only in their rate of discharge, the resulting chamber contraction, and the degree of existing A-V block. The fastest rate of discharge results in auricular fibrillation, the next most rapid gives rise to auricular flutter, and the slowest ectopic rhythm causes paroxysmal auricular tachycardia. The ventricular response is, of course, dependent on the rate of auricular discharge and the degree of A-V block.

These arrhythmias may be paroxysmal or sustained. They are usually associated with organic disease but not infrequently occur in apparently normal people.

Auricular fibrillation—(1) Paroxysmal, of short duration and not associated with advanced heart disease: quinidine sulfate by mouth in doses ranging from 0.2 to 0.8 mg. every two to three hours until normal sinus rhythm is restored. (2) Long duration and associated with serious organic disease: digitalization sufficient to maintain ventricular rate below 80 to 90 per minute.

Auricular flutter—(1) Digitalize, then the withdrawal of digitalis will often convert auricular flutter to auricular fibrillation and reversion to normal sinus rhythm may spontaneously occur. Intractable cases may require the combined use of digitalis and quinidine. Some extremely resistant cases may have to be maintained on digitalis which controls ventricular rate as in auricular fibrillation.

Paroxysmal ventricular tachycardia: (The most dangerous of cardiac arrhythmias except ventricular fibrillation.) Be sure to exclude excess digitalization as a causative factor. Quinidine lactate 0.65 mg. is now available for intravenous use in 10 cc. ampules (Lilly) and this obviates the necessity of the cumbersome preparation of quinidine for intravenous therapy. The drug must be given slowly and if respiratory or circulatory collapse occurs, caffeine sodium benzoate should be given intravenously. Following restoration to normal rhythm, quinidine sulfate should be given in 0.2 to 0.6 gm. doses by mouth every three hours for three to four days.

If cardiac failure is associated with this arrhythmia and if digitalis has not previously been given, the patient should then be digitalized.

Digitalis: Powdered whole leaf versus the glucosides—When digitalis is indicated in the treatment of the arrhythmias discussed, the following factors will determine the preparation most suitable.

For rapid intravenous administration: lanatosid C. 1.6 mg. intravenously or digitoxin 1.2 mg. intravenously. (Be sure that patient has not previously been given digitalis.)

For rapid oral administration: digitoxin 1.2 mg. followed by a maintenance dose of 0.1 to 0.2 mg. every twenty-four hours.

When haste is not a factor or when digitalis effect is to be maintained for an indefinite period, either the tablets of the glucosides or the whole leaf preparation may be used with equal efficiency.

Quinidine sulfate: Usually given by mouth in doses of 0.3 to 0.6 gm. every three to four hours. Larger single doses of 0.8 gm. have been shown[2,3] to produce higher blood levels more rapidly and to sustain the levels longer than the same amounts of quinidine given in smaller, more frequent doses. Effective blood levels may exist for ten hours by this method of administration.

Quinidine may provoke sensitivity reactions in some individuals. A similar effect without reaction may sometimes be obtained wtih atabrine.[4] The drug is best administered by dissolving 0.6 gm. in 10 cc. of 1 per cent novocain and given intramuscularly or 0.1 to 0.2 gm. may be dissolved in 10 to 20 cc. normal saline and given intramuscularly every hour until 0.6 gm. has been given. Maximum blood level is reached in fifty-five to eighty-five minutes.

If quinidine has previously been administered, allow six hours to elapse before giving atabrine. This procedure is sometimes effective when quinidine has failed.

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Treatment of Osteomyelitis

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Students of osteomyelitis have averred from the statistical material available that in recent years this disease has become less virulent and less severe than in the past. However, no matter how convincing their investigations may be, it is quite plausible to assume that the response of this disease to recent methods of treatment may be in part responsible for its appearing less severe.

Generally speaking, inflammatory lesions of the bone may be considered as acute or chronic, mild or severe. The pathology may be sharply localized or widely diffused in the bone, and even metastasize to other parts of the body. It may affect the marrow cavity, cortex, periosteum, or all of them if allowed to progress a sufficient length of time. The extent of advancement of the process when treatment begins is in direct relation to how long the patient has suffered prior to adequate medical attention, or how alert the physician who is attending him has been in apprehending the condition, making a diagnosis, and instituting the treatment.

In other words, the earlier diagnosis is made and treatment instituted, the better is the possibility of limiting the progress and advancement of the disease. When a child complains of pain in the extremity, the physician should be on the lookout for osteomyelitis. By an early diagnosis and proper treatment, one may abort an otherwise serious condition.

Hematogenous osteomyelitis is an acute condition resulting from a bacteremia and occurring most often in childhood. Usually it begins with the symptoms of pain, limp, rise in temperature, swelling, and even redness in the region of the metaphyseal ends of the diaphyses of long bones (the order of frequency is temur, tibia, humerus, radius). There is an acute exudative inflammation of the marrow, a local thrombosis and obliteration of vessels which leads to necrosis and the formation of toxic exudate. This spreads through the vascularized channels to reach the external surface of the cortex, dissecting and raising the periosteum (subperiosteal abscess) further damaging blood supply.

Unless this pathologic process is arrested early by chemotherapy, immobilization, and perhaps surgical drainage, the infection tends to spread and metastasize. It is with the knowledge and recognition of this pathologic picture that the proper program of treatment can be instituted. In other words, from the history and the physical and clinical findings, one can tell considerable regarding the extent of the pathology.

Let us take the example of R. S., a boy 8 years of age. He came home from school one afternoon limping. He had a painful stiffness about his ankle. His parents thought he had a fever. The next morning he had an emesis after breakfast and could hardly bear weight on his leg. His parents carefully kept him in bed that day. He had a fretful night with pain in his

leg. The following morning the pain was greater. There was slight swelling in the lower leg. They took him to a physician who found that his temperature was 102.4° F.; white blood cell count was 14,200; sedimentation 30. X-ray examination was negative. Localized tenderness was sufficient to convince the physician of the diagnosis of osteomyelitis.

He was placed in the hospital where his leg was splinted. Ice bags were applied about the ankle, and 300,000 units of penicillin were given him immediately. Adequate doses of sulfathiazole were also administered and fluid intake encouraged. The next day, although the temperature was normal, a second 300,000-unit dose of penicillin was given. By the third day there was no pain or swelling, but 100,000 units of penicillin were given every three hours for the three following days, making five days of rather heavy dosage of penicillin.

The boy was up on crutches in two weeks; in four weeks a check-up x-ray showed nothing abnormal in the bone, and he was allowed to bear weight, apparently completely cured. An x-ray three months after the attack showed a slight periosteal ossification thickening which ultimately disappeared.

This is not an exceptional case. It simply illustrates the importance of early recognition and proper management before the process has done more than filtrate through the wide haversian canals of a child. On the other hand, if this child had been allowed to be up and around and active, and not had prompt chemotherapy, his course might have been very different. We might have had local abscess formation, incision, secondary infection, a long history of local and remote draining sinuses, with recurrences in the form of chronic osteomyelitis. Of course, we cannot expect every case to respond as serenely as our example.

Sometimes we will find unusual changes in apparently cured cases, such as evidence of decalcification and apparent bone necrosis in late x-rays. The importance of such findings of suspicious dead and sequestrating bone is directly dependent upon whether the patient also has symptoms of pain, tenderness, or elevated temperature that might lead one to suspect an active infective process. If such symptoms are not present, it is far better to regard this condition expectantly; usually the x-ray changes finally disappear. If there is evidence of infection, one must consider the resumption of chemotherapy and possibly operation. In our early experience with chemotherapy, we became very alarmed over these extensive x-ray changes with shadows of sequestrum and involucrum. But we finally became aware that these were but a part of the bone replacement program following extensive damage due to the infection.

Most parents are becoming aware of the opportunities afforded by early recognition and treatment of bone disease in children. Occasionally some revert back to poultices, "drawing" salves, and liniments, with aspirin as a sedative; it is from this group that one sees late changes such as subperiosteal abscesses and extensive damage to the bone. Some very early cases of osteomyelitis, depending on the virulence of the infection, are aborted simply by quiet, rest, and immobilization, with general supportive care of the patient. But unless they abort, the pathologic course continues in every case, and may require not only chemotherapy, but also surgery.

SURGICAL TREATMENT

There are certain fairly well established rules with respect to surgical treatment of osteomyelitis which, if followed, will usually avert pitfalls of disaster. We shall briefly outline them in the order of their importance.

1. Before any operative procedure is considered, the patient should be "filled" with the proper chemotherapeutic agent.

If possible, one should determine whether the bacteria are susceptible to penicillin, streptomycin, or the sulfonamides. This may be accomplished through aspiration, examination, and blood culture, but it would be far better to give penicillin and one of the sulfonamide drugs immediately than to await the result of a culture.

Dosage to the therapeutic limit (determined by age, size, and virulence) of such agent should be given.

Dosage should be continued for one or two weeks after clinical evidence of infection has stopped. As long as there is evidence of infection, massive doses should be continued. Later when symptoms have abated the dosage may be reduced.

If sulfonamide drugs are used, adequate fluid intake is essential.

2. **Rest.** A plaster of paris splint or some type of immobilization in a position of optimum function is desirable before any operative procedure, and absolutely essential after operation. The entire extremity should be placed in a plaster of paris cast which is bivalved, so that intermittent examination of the diseased area can be made without disturbing the extremity. Ice bags placed about the inflamed area are advisable.

3. **Operation.** A. Surgical procedures should be delayed at least twenty-four hours to allow the patient to be filled or saturated with the proper chemotherapeutic agent. This delay and therapy have saved many from incision.

B. During this period an estimation of the patient's local and general condition can be assayed, and if necessary, intervenous fluids and transfusions can be given.

C. Sometimes subperiosteal aspiration is helpful as a therapeutic measure, and may prove a turning point to recovery, making operation unnecessary.

D. The type of operation performed depends on the patient's general condition, age, and the findings in the x-ray at the time of operation.

Little children should have the least surgery. Aspiration, incision, drainage through periosteum, or perhaps drilling of the cortex is usually adequate. If incision is necessary, careful irrigation of the abscess with normal salt solution to remove the exudate is appropriate. The local application of penicillin, and perhaps an irrigation tube for penicillin in the wound may be used but should be withdrawn in forty-eight to seventy-two hours. If well cleaned up, loose closure of tissues is advised.

Older children and adults with severe infections sometimes require saucerization or removal of all the diseased bone. The area should be carefully cleansed of debris and exudate, then given a cover of muscle tissue, and a loose closure of the skin. Some advise irrigation with penicillin for a few days. Immobilization should be carried out and a bivalved plaster cast should be worn until the wound has healed.

E. Postoperatively, heavy doses of penicillin or other appropriate chemotherapy should continue as long as evidence of infection is present. Then smaller doses can be given for three, four, or more weeks. It is difficult to know exactly when all the bacteria have been destroyed.

Chronic osteomyelitis occurs when acute osteomyelitis has apparently been cured and the bacteria live in a quiescent state within the primary focus and cause exacerbations of the condition by activation and extension from its original focus. Or they may be carried in the blood to a distant part and metastasize. We often see chronic osteomyelitis after compound fractures.

It is useless to try to cure chronic osteomyelitis with chemotherapy alone, as the agent cannot reach the bacteria within their focus of necrotic bone. Therefore, radical operative procedure is usually indicated.

Before any operative procedure is considered, the patient must be filled with penicillin or other appropriate chemotherapeutic agent to the limit, at least for twenty-four hours prior to operative intervention. Complete removal of every particle of diseased bone, exudate, and debris is essential by thorough saucerization of the area. Thorough irrigation and cleansing with salt solution and hydrogen peroxide is indicated to assure a complete cleanup. A generous application of the chemotherapeutic agent may be used locally. If possible, a muscle covering should completely overlie the denuded bone area. Skin should be closed loosely and cast applied and bivalved as previously described. Again, the patient must be hit hard with chemotherapy to the therapeutic limit for at least a week postoperatively.

The end results in all these conditions may not be all you desire, but will largely depend upon (1) the early recognition of the condition; (2) the institution of early chemotherapy in adequate appropriate doses; (3) the preoperative preparation of the patient, if operation is indicated; (4) the meticulous and thorough surgical technic that is used; (5) the postoperative management and follow-up of the patient.

Present Concepts of the

Treatment of Dental Caries

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Dental caries is a disease of the calcified tissues of the teeth. It is caused by acids resulting from the action of microorganisms on carbohydrates and is characterized by a decalcification of the inorganic portion which is accompanied or followed by a disintegration of the organic substance of the tooth.

Treatment is necessarily divided into two methods: that of restoration, by means of artificial materials, of carious lesions or developmental defects which may be precursors of lesions, and that of prevention.

The caries-susceptible individual can be benefited greatly in the direction of future protection by proper operative dentistry for the lesions already created and anticipatory correction of deep pits and fissures in the occlusal surfaces. The adjustment of the arrangement of teeth to comply with a reasonable arch form for the given individual will also contribute much to reducing the future susceptibility to caries.

The field of caries prevention is concerned with the inhibition of one or all of the known factors in the etiologic process. All of the effective acid is derived by means of bacterial enzymatic action upon the carbohydrate left in the mouth after it has been ingested. The effectiveness of the acid depends on whether or not it is neutralized

before decalcifying the teeth. This in turn depends upon the rate of formation, the rate of neutralization, and the amount of carbohydrate ingested.

The Lactobacillus acidophilus is now established as the member of the oral flora responsible for the production of harmful acid, and saliva counts of Lactobacillus are used as an index of caries activity. The ability of the acid to decalcify the inorganic material of tooth enamel is regulated by its relative perviousness, and certain developmental channels (lamellae) are credited with being passageways for the ingress of proteolytic bacteria to produce dissolution of the organic matrix.

The above are the known salient factors in the production of caries and upon which the present concepts of treatment for prevention are based. The quality and quantity of saliva are controlled by nutrition and the sympathetic nervous system. On this basis, an alkaline ash diet should decrease caries activity in some cases, due to a more alkaline saliva. This has not been found to be an effective mass control, probably because of the variability in the individual in many factors.

Restriction of carbohydrate in the diet, especially by eliminating the refined sugars, is an effective control of caries activity. This operates by eliminating the substrate in the oral cavity upon which the microbial enzymes act and a growth factor of the bacteria.

Careful studies at the University of Michigan and the University of California have shown that drastic reduction of refined sugars for limited periods of time will definitely reduce the lactobacillus count. After varying periods of such carbohydrate reduction the patients are allowed a small amount of refined sugar at one meal per day and a continued low bacterial count and caries index are maintained.

Studies at the University of Iowa have shown that an adequate diet which meets the requirements of the body will serve to prevent dental caries as well. This adequate diet is also low in sugar and there are several reports of studies made during the war in which diets very inadequate nutritionally and also lacking in sugar produced a definite reduction in caries activity.

Throughout the consideration of the effectiveness of various means of caries control the difference in approach, that of mass or individual, must be kept in mind. The restriction of refined sugars in the diet is a control of the individual and must be done with the cooperation of the patient and physician.

ACTION OF FLUORINE

It has been known for some time and conclusively reported that in areas where the communal water supply accidentally contained fluorine, the rate of caries activity was much lower than in those areas in which it was not present. Fluorine over 2 parts per million will produce developmental defects in the teeth (mottled teeth) but these teeth are even less susceptible to caries than well-developed teeth in nonfluorine areas. This consequently presents a possibility of mass control and to this end sodium fluoride is being added to the water supplies of various communities throughout the country.

Evanston, Illinois, represents such a community. Since February 11, 1947, sodium fluoride at the safe rate of 1 part per million has been added to the water supply and daily determinations are made both at the filtration and distribution points with only a 2 per cent variable. These projects are under the close supervision of the National Institutes of Health which checked the possibilities of such a procedure experimentally with good results before advising it on a larger scale. It is too early for the results of this study to be significant.

The fact remains that it is not known whether or not the artificial addition of fluoride to the water supply will produce the same results observed in areas in which fluorine occurs naturally. Furthermore, it is difficult to conceive the possibility of fluorine taken internally affecting the caries susceptibility of teeth already calcified. The rationale of this treatment is based upon the assumption that the addition of the fluorine ion to the structure of the enamel during the developmental period will render it more impervious to the inroads of acid. It has been shown in fluorine areas that noncarious teeth contain a greater percentage of fluorine than carious teeth in nonfluorinated areas.

A topical application of a 2 per cent solution of sodium fluoride, by means of a definite technic and repeated applications, has been shown by the U. S. Public Health Service to be effective in children up to 15 years of age. They report a 40 per cent reduction of caries but this result must be evaluated on the basis of *individual reaction* rather than mass statistics, since the number of variables in the treatment makes it impossible to promise the same result for any particular individual. No beneficial results have been reported for the same treatment of adults.

The mode of action of fluorine in this respect may be attributed to enzyme inhibition, reduction in the solubility of the teeth, or inhibition of bacterial growth, or all three together. The reduction in solubility may be produced by changing the hydroxyapatite of the enamel to the more acid-resisting fluorapatite. The duration of the effect of topical application of fluoride is not known.

Sodium fluoride used in mouth washes, chewing gum, or chewed and ingested in tablet form has been repeatedly shown to be ineffective in the reduction of caries activity.

AMMONIUM ION EFFECT

Approaching the problem from the standpoint of inhibiting the growth of lactobacilli, it was found that caries-immune saliva contained ammonia in a higher percentage than caries-susceptible saliva. Workers at the University of Illinois gathered evidence and theorized that the ammonium ion retards the growth of Lactobacillus. This factor allowed the entrenchment of Bacterium aerogenes which produces an enzyme capable of deaminizing the amino acids, thus liberating ammonia and further impeding the lactobacilli.

A dentifrice was compounded containing dibasic ammonium phosphate and carbamide or urea (to increase the buffering capacity of the saliva) and used in controlled groups of children under strict supervision with apparently good results. A more extensive program of clinical evidence should be forthcoming before the reduction in Lactobacillus counts and reduction of caries activity by this method can be definitely established. This treatment is possible for both mass and individual application.

Antibiotics such as penicillin have been incorporated within a dentifrice to alter the oral flora and have been shown to reduce Lactobacillus counts. No clinical data concerning caries reduction are available and the controversy stimulated by allergists in respect to the regular use of penicillin has not been conducive to establishing such data.

Investigators at Baylor University and others have explored the possibility of the invasion of microorganisms along unobstructed organic roads (enamel lamellae). Immune persons apparently have calcium deposited in these channels by the enzymatic action of phosphatase. On this basis and the theory that the invading organisms are essentially proteolytic, a technic of impregnation is used to coagulate the protein contained therein and fill invasion roads. Zinc chloride, 40 per cent, is applied to all surfaces of the tooth and followed by potassium ferrocyanide, 20 per cent, applied in the same manner.

This treatment is effective in reducing the sensitivity of certain areas of the teeth. Substantial reduction in the rate of caries activity and in the Lactobacillus count, due to the elimination of open entrances of the organic invasion roads, has been reported. Insufficient clinical evidence and controlled data, however, make it impossible properly to evaluate this hypothesis at this time. It has been shown that the tooth enamel matrix contains an acid-soluble carbohydrate protein complex which could be removed concurrently with the inorganic material in the aciduric process.

The impregnation of tooth surfaces with silver nitrate has been used for a long time in an effort to control caries activity. The reports in the literature are conflicting and the fact that the technic is a highly individualized one in addition to causing discoloration of the teeth has not led to its general acceptance.

The possibility of introducing a nontoxic enzyme inhibitor into fermentable sugars during their manufacture has been advocated and explored by workers at Northwestern University. This would present an effective mass control. They have incorporated such an enzyme inhibitor, vitamin K, in chewing gum and evidence has been introduced showing that it has a caries-inhibiting effect. Although theoretically sound, the practicality of this procedure has not been properly demonstrated.

SUMMARY

The study of preventive measures for dental caries in the last decade has produced a voluminous literature and while the exact etiology is still elusive, a great deal is now known concerning the control of pertinent factors in the caries mechanism.

Dental caries activity can be greatly reduced by the use of diets low in refined sugar, but which meet the nutritional requirements for good health.

The topical application of sodium fluoride gives promise of reducing caries in children up to 15 years of age.

Good operative dentistry can and does contribute much to the prevention and curtailment of caries activity.

The future possibilities are reduction of caries by means of fluorination of public water supplies, the use of dibasic ammonium phosphate and urea in dentifrices, and the incorporation of enzyme inhibitors in fermentable sugars. The technic of impregnating enamel lamellae with protein coagulants awaits basic and clinical confirmation.

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UPROAR ABOUT MEDICAL EDUCATION OR "WHAT'S ALL THE SHOOTIN' FOR?"

In January the Academic Deans of some of our colleges and universities held a conference in Cincinnati and passed the kind of resolutions one might expect from freshmen students rather than academic deans. One dean from Northwestern University tried a little name calling and innuendo. Another dean from Ohio State University cited some grossly inaccurate figures to support a somewhat weak case. Apparently the deans believe there is a serious shortage of doctors, that there is insufficient competition to maintain a high quality of education or medical service; that research suffers because some thousands of qualified young men do not get into medical school.

All this opinion seems to have been offered without supporting evidence. Fortunately Dean Joseph C. Hinsey of the Cornell University Medical College, who is also president of the Association of American Medical Colleges, provided an excellent answer in a letter to the New York *Times*. Unfortunately his excellent analysis was not widely circulated by the press associations that circulated the preposterous accusations voiced by Academic Deans Leland and Guthrie.

Dean Hinsey pointed out that Dean Guthrie said there were 6,387 places open in freshman classes whereas there were actually 6,986 students enrolled in freshman classes this year, an increase of 9 per cent over last year. Dean Hinsey wondered if Dean Guthrie was advocating a return to the "diploma mills" and low grade education of 1905. Dean Hinsey said that the mortality rate in medical education of 3 to 5 per cent cited by Dean Leland was actually near to 10 or 15 per cent and that a saving of even 5 per cent in this attrition rate would be equivalent to the establishment of three or four new medical schools. Dean Hinsey also called Dean Leland's attention to the fact that the number of physicians has increased more rapidly than has the population of the country as proved by Dean Willard C. Rappleye of Columbia University and he remarks that Dean Rappleye's experience in medical education qualifies him as a better judge than Dean Leland.

Next Dean Hinsey notes that new medical schools or expansions of two-year schools have been developed in Alabama, Washington, California, Texas, North Carolina, Utah and Illinois; others are being considered in Mississippi, Florida, West Virginia, North Carolina and elsewhere. Dr. Victor

Johnson, director of the Mayo Foundation, has shown that there is an annual increment of about 2,000 physicians to the profession, in the excess of graduates over the physicians who die during the year.

Dean Hinsey rebukes Dean Leland for his "undignified implications"—plain misstatements of fact I would call them—and he asks the academic dean to realize that medical education is in the hands of medical educators who are just as devoted to their field as he is to his.

In his concluding paragraph Dean Hinsey says just about all that needed to be said about this peculiar eruption from the academic deans. "Medical education is not perfect," says Dean Hinsey. "No one knows this better than medical educators. We are trying to keep our house in order, as is evidenced by the survey." (Now being made by the A.M.A. Council on Medical Education and the Association of American Medical Colleges.) "We have been the targets of politicians, at times even of the medical profession, and now of our colleagues: some, I hope just a few, of the academic deans. Medical education is the foundation stone of our national health, and the public must appreciate that, without sound undergraduate medical education of high quality, we cannot maintain and advance our program of medical research and medical care."

That's telling 'em, Dean Hinsey, and all the medical deans owe you a vote of thanks for saying what needed to be said and saying it so well.

MORRIS FISHBEIN

A PATTERN FOR HOSPITAL CARE

DURING most of 1949 a group working under the direction of Dr. Eli Ginzberg of Columbia University made a comprehensive study of hospital care in the state of New York.* Their report, published in December, 1949, is a revealing document, culminating in a series of recommendations as to the responsibilities of state and local governments and of voluntary groups in the field concerned. The last recommendation to the voluntary groups merits first quotation here:

> "Voluntary groups should take cognizance of the significant role of government in the provision of hospital care, and realize that a well-functioning and efficient hospital system for the community at large depends on the cooperation of voluntary and governmental groups working in the public interest."

Some important observations should be emphasized. The experts estimate that an enrollment of 85 per cent of the population is an appropriate target for voluntary insurance against the costs of medical care, including hospitalization. Only 15 per cent of the people need to be looked after by the government and charity. Instead of the conventional twenty-one days of full coverage by Blue Cross Plans, the report favors a ninety-day maximum.

The committee feels that Blue Cross Plans should eliminate exclusions, particularly as to diagnostic x-ray services and that experiments should be under way to test possibility of enrolling individuals, caring for the aged, and providing diagnostic services. If the target figure of 85 per cent has not been approximated in several years, the committee says the public must consider the advantages of adopting a system of compulsory hospital insurance to be integrated with the existing pattern of workmen's compensation and cash sickness insurance.

With a view to improving efficiency of hospitals and lowering costs, small hospitals should not be replaced as they become obsolete and specialistic services should be provided through use of the part-time plan. Inefficiency seems to result from boards of trustees who do not use their power properly; administrators who have responsibility without power and medical boards which have no specific responsibility or power but exercise control; at least that's what the committee report says!

Special emphasis is placed on expanding

*GINZBERG, ELI: A Pattern for Hospital Care, Final Report of the New York State Hospital Study. Columbia University Press, New York, 1949, pp. 368. $4.50.

services to ambulatory patients, in the interest of lowering costs, improving early detection of disease, and utilizing group practice units.

As might have been expected, the problems of medical care and hospitalization loom especially large. The number of recommendations in this field is large and runs a course from mental hygiene beginning in infancy to new hospitals, ambulatory services in centers, education of more personnel, increased salary scales, and support of research.

Especially interesting at this time when public relations advisors are urging medical societies to set up grievance committees to hear complaints of the public against doctors and hospitals is a recommendation that the state establish a hearing system for *aggrieved physicians:*

> "Because most doctors need a hospital affiliation if they are to practice good medicine and grow professionally, and because boards of trustees of voluntary hospitals on occasion exercise their powers of appointment to hospital staffs in a manner opposed to the public interest, it is recommended that the State establish a hearing system for aggrieved physicians. When indicated, the findings of such hearings should be published in the hope that hospitals will become more responsible in discharging their civic trust."

Altogether this report is one of the most valuable documents ever to come from any such study group. Its pages are replete with important discussions that need to be read and studied carefully by everyone interested in the maintenance of our voluntary hospital system and in the high standard of care of the sick that prevails in our country.

MORRIS FISHBEIN

THE ADRENAL CORTEX IN ARTHRITIS

Professor Hans Selye of the Institute of Experimental Medicine and Surgery in the University of Montreal, contributed to the *British Medical Journal* of November 19, 1949, a report of his early work on the participation of adrenal cortex in the pathogenesis of arthritis.

Selye seems to have been first to put forward the idea that the adrenal cortex plays an important role in the pathogenesis of rheumatic and rheumatoid conditions in men. This he did in an article published in the *Journal of the American Medical Association* (1944, 124:201).

Investigations indicate that the response of the human organism to a variety of stress-producing agents such as emotional tensions, infections, intoxications, and exposure to cold includes an increased production of the hormones of the cortex of the adrenal gland. This, Selye proved in 1937, helps to raise the resistance of the body in general. Selye has developed a simple technic for producing arthritic and periarthritic changes. With this method he has been able to analyze the role of the pituitary adreno-cortico system in the production and prevention of arthritis. An alarm reaction produced by cold, forced muscular exercise or similar trauma increases resistance against the edema of the lungs that can be produced by poisonous doses of adrenalin or anaphylactic shock. Experiments in the rat have shown that anaphylactic reactions from egg white can be inhibited by injections of ACTH and Cortisone. Selye emphasizes that the anti-arthritic effect of ACTH and Cortisone is not a specific action against some hypothetical cause of rheumatoid or arthritic joint lesions. ACTH has proved to be effective in gouty arthritis.

The experiments of Selye and others prove that even the arthritis caused by a non-specific inflammatory agent, such as formaldehyde, can be effectively prevented by ACTH and Cortisone. Formaldehyde arthritis is produced by injecting this toxic agent into the vicinity of joints. If large doses of formaldehyde are thus injected, the acute stage is followed by a prolonged chronic arthritis with such manifestations as edema and pronounced proliferation of the connective tissue, also stiffening of the joints, and swelling of the surrounding skin. This arthritis is slightly aggravated by treatment

with desoxycorticosterone acetate. However, it can be almost completely inhibited by Cortisone and ACTH. Thus, according to Selye, there seems to exist an antagonistic relationship between DCA or crude anterior pituitary preparations on the one hand and ACTH on the other.

MORRIS FISHBEIN

A CALL TO FREEDOM

Among the great in the history of medicine was Sir James Paget, noted pathologist and surgeon. In August, 1882, Sir James delivered an address at the Jubilee meeting of the British Medical Association in London. His words still echo as a warning to physicians—a warning which apparently went unheeded by the medical profession of Great Britain. He said:

> I hold that our great anxiety, our great strife, should be, to be a self governed profession; to know our own wants, and not to go to others to help us; to find out the remedies for ourselves; to find out by careful, patient controversy, and mutual concessions, how we may, without any external help, bring about the results which the best and the largest number of us wish for. Let us be, as all highly cultivated persons should be, self governed. No one can know so well as ourselves, our need; none can know so well the remedy we require. It tells of feebleness, of cowardice, and want of self-reliance when we want to go to any Parliament living to help us.

The problems that confront the medical profession of the United States today can be solved properly only by the medical profession itself. The list includes the unsolved difficulties of medical education, the problems of the hospitals, the provision of medical care, and the advancement of medical knowledge through research.

Apparently government is willing to provide funds which medicine can receive only when the funds are granted without government domination. Yet it is not in history that governments give unless they can govern! The impasse could be resolved without sacrifice of principle if leaders of government recognized the essential character of sound medical guidance and leadership.

MORRIS FISHBEIN

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The Medical Bookman

TEXT-BOOK OF OPHTHALMOLOGY*

When Duke-Elder published his first volume in 1932 he did a great service to English-speaking practitioners. Prior to that time no reference text-book in ophthalmology existed in the English literature. For a person to be well-trained it was necessary that he be familiar with the foreign languages.

Since their publication the preceding volumes have assumed a position of such eminence that hardly an article appears in our ophthalmologic literature today that does not contain some reference to the works of Duke-Elder. This volume continues the same high standard. There are numerous, pertinent illustrations, both pictorial and diagrammatic. The chapters, and frequently divisions within each chapter, are followed by very comprehensive bibliographies.

The book is divided into three sections: The Neurology of Vision, Motor Anomalies of the Eyes, and Optical Anomalies of the Eye. As in his other volumes, the author introduces each section and most of the chapters by a picture and biographical sketch of the man he feels has contributed most to that particular subject.

The author begins with a comprehensive study of lesions which may involve the visual pathways. He starts at the chiasm and continues along the optic tract, the external geniculate body, the optic radiations, and the visual cortex. In masterful fashion Duke-Elder discusses pituitary lesions, suprasellar tumors, presellar tumors and parasellar tumors. In discussing vascular lesions, he re-emphasizes the fact that almost any aneurysm of the arteries in the region of the circle of Willis may compress some part of the visual pathway and cause progressive changes in the fields of vision (Figure 2995). In addition to describing the findings essential to a diagnosis the author suggests methods of treatment.

From the chiasmal pathway Duke-Elder passes to lesions involving the basal visual pathways and the intracerebral visual pathways. With some apology for not including the disease in his third volume the author undertakes a complete discussion of toxoplasmosis. He gives full credit to American workers for recognizing the importance of this new clinical entity.

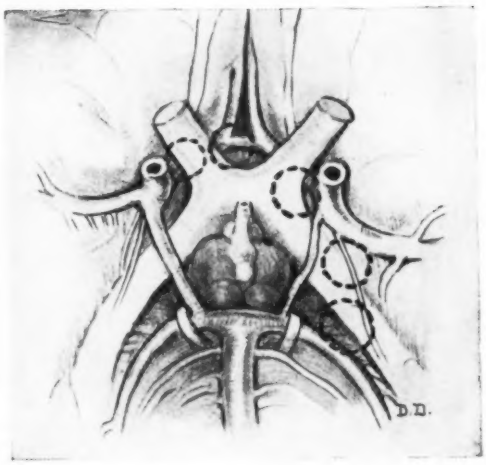

FIGURE 2995. Diagram illustrating the common sites of aneurysms and their relation to the chiasmal pathways (Jefferson, *Brain*).

Chapter 43 is concerned with disorders of the higher visual centers. The author's obvious delight in this subject is manifest in the opening paragraph:

> With the exception of Chapter XXVII, which dealt with the physiology of the perceptual processes of vision, this is the most exciting chapter of this text-book to write. This is because it deals not with observational facts and topographical studies of disease processes which are amenable—within the limits of our knowledge—to detailed factual description, but with the much more intellectually intriguing exercise of synthesizing general conclusions from observations carried out upon a plastic and labile mechanism of which, in health, and even more so in disease, we are still profoundly ignorant.

This chapter begins with a description of the

*Text-Book of Ophthalmology, Vol. IV, The Neurology of Vision, Motor and Optical Anomalies, by Sir W. Stewart Duke-Elder. 1154 pages with 1081 illustrations, including 71 in color. 1949, C. V. Mosby Co., St. Louis. $20.00.

FIGURES 3086-87. Visual agnosia. A very delightful illustration of visual agnosia. The distress of the little old lady at not recognizing a well-known object is apparent (Figure 3086); her relief at recognizing it by touch is as evident (Figure 3087). *Illustrations from: "Text-Book of Ophthalmology," by Duke-Elder.*

organization of the brain and continues with a discussion of visuo-sensory disorders and associational disorders. The author defines agnosia as the inability to recognize or orient objects which are perceived although the reception of their sensory impressions is intact. He discusses visual agnosia and includes a relevant illustration (Figures 3086-87). The chapter continues with a discussion of paroxysmal disorders, disorders of perception, and psychogenic disorders.

Next the author devotes a chapter to the discussion of anomalies of the pupillary pathways. He defines a typical Argyll Robertson pupil as one characterized by (1) complete immobility to light, (2) unimpaired or increased response to the near reflex and the lid reflex and (3) a miosis of less than 3 mm. In disagreement with some authorities Duke-Elder feels that the pupils react both in convergence and in accommodation although he does feel that the convergence reflex is more potent. The chapter closes with a discussion of abnormal pupillary reactions.

Section 15 is of primary interest to ophthalmologists and neurologists. The first chapter is directed to anomalies of the ocular movements. The classification of these movements is sometimes confusing. The author helps clarify this situation with an excellent illustration (Figure 3177) of monocular and binocular movements. He then proceeds to a discussion of the evolutionary development of the fixation reflexes. An infant does not develop conjugate fixation until the age of 5 to 6 weeks. Conjugate deviations do not become completely accurate until the age of 6 months. It is not until the age of 5 years that the reflexes begin to acquire the fixity comparable to that of an unconditioned reflex.

The author has reversed his opinion as to the presence of a center for divergence since publishing his first volume. He is now in accord with the advocates of such a center and localizes it as a subcortical center (or at least an association area) situated probably in the midline in the neighborhood of the VIth nerve nucleus.

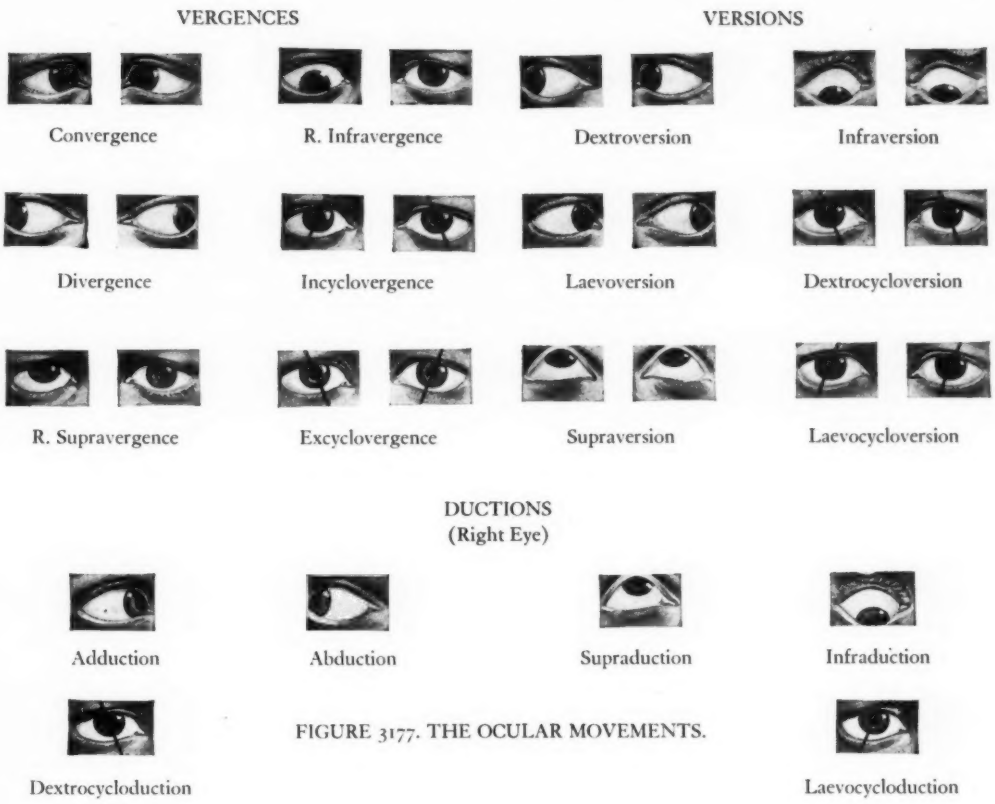

FIGURE 3177. THE OCULAR MOVEMENTS.

Duke-Elder discusses the general symptomatology of strabismus, elaborating upon the significance of Worth's classification of fusion into three grades and upon the technic of testing for these. Considerable space is given to an evaluation of the clinical methods of investigating a case of squint. He describes the Hering after-image test, the congruence test of Tschermak and the use of the major amblyoscope in determining the state of retinal correspondence. The chapter ends with a review of the general treatment of strabismus.

Chapter 46 provides a more detailed discussion of anomalies of binocular fixation. The author describes anomalies both of conjugate fixation and of disjunctive fixation.

The next two chapters cover a comprehensive analysis of concomitant squint and noncomitant squint, respectively. Duke-Elder differentiates ocular torticollis from orthopedic torticollis and states that the presence of the former can almost be accepted as a diagnostic indication of a congenital or early infantile palsy. The author includes a detailed discussion of acquired ophthalmoplegias of nervous origin. He describes a system for localizing neurogenic ocular lesions as supranuclear, nuclear, stem, root or trunk palsies.

The last two chapters are entitled, "Ocular Deviations" and "Pathological Nystagmus." Agreeing that the central connections of the oculomotor nuclei are of considerable complexity, the ramifications of which have not yet been made clear, the author discusses the subject under the headings of the frontal mechanism controlling voluntary conjugate movements, the disjunctive deviations, the occipital mechanism controlling visual reflex movements, and the extrapyramidal system. His discussion of nystagmus is subdivided into ocular, vestibular, central, idiopathic, congenital and voluntary and hysterical nystagmus.

The Third Section concerns itself with optical anomalies of the eye. Errors of refraction are classified as simple, pathologic, and transient. There is a prevalent misconception that because myopic eyes are usually large eyes they are almost never afflicted

with glaucoma. It is, therefore, to the point to quote the author: "A significant percentage of cases of glaucoma, usually of the slow, insidious, and chronic type, occur in high myopia, most observers giving a figure of about 14 per cent."

Duke-Elder discusses the pros and cons for refracting with cycloplegia. He relegates subjective refractive methods to the role of a *prove-up* regarding their use as a primary procedure as worthy only of the department store. To those of us who are familiar with dynamic refraction as advocated by Dr. W. B. Lancaster this is heresy. Dr. Lancaster's method is very valuable and, in certain cases, superior to objective methods of refraction. Apart from this, the author gives an excellent discussion of objective methods of refraction and evaluates the technic of ophthalmoscopy, retinoscopy, refractometry, and keratometry.

In a chapter on anomalies of accommodation, there is a complete discussion of paralysis of accommodation. As the author states, this condition may be unilateral or bilateral, sudden or insidious in onset, and may be due to a congenital anomaly, to the action of drugs, or to infective, toxic, nervous or traumatic causes.

He assigns a chapter to aniseikonia, a concept which is just beginning to assume a role of importance in clinical ophthalmology. Another chapter concerns eye-strain and visual hygiene. The symptoms of eye-strain are divided into visual, ocular, referred and functional. It is interesting to note that in addition to the well-known referred symptom of headache, gastric manifestations are very common. In discussing the treatment of eye-strain, the author says, "Nothing is more pernicious than the routine correction of optical defects by rule-of-thumb methods. Not only is the eye to be treated as an optical instrument, but it ought always to be considered as an integral part of the body, sharing with other organs in its constitutional variations and in the effects of the ills with which it may be afflicted."

The final chapter of this volume relates to clinical optical appliances. The author discusses the optics of spectacle lenses and mentions the optical defects of spectacles. Happily the tolerance of the eye is considerable so that many of the aberrations can be neglected. For the important remaining conditions, he considers the characteristics of a "best form" lens. Duke-Elder concludes with an appraisal of compound lens systems (telescopic and anisometropic spectacles), contact lenses, miscellaneous optical appliances (magnifying lenses, prismatic spectacles, etc.) and protective glasses.

P. B. J.

New Books Received

► THE 1949 YEAR BOOK OF RADIOLOGY - - -

Edited by Fred Jenner Hodges, M.D., Professor and Chairman of the Department; John Floyd Holt, M.D., Associate Professor, and Isadore Lampe, M.D., Associate Professor, all of the Department of Roentgenology, University of Michigan, Ann Arbor. 480 pages, with 400 illustrations. 1949, Year Book Publishers, Inc., Chicago. $6.50.

From the most outstanding articles on roentgenology, published in 1949, the editors have abstracted the highlights for reproduction in this volume.

The subject of "Roentgen Diagnosis," presented in the first half of the book, is subdivided into: (1) technical developments, (2) head, (3) spine and extremities, (4) chest, (5) gastrointestinal tract, and (6) genitourinary tract. There are discussions of amplification of fluoroscopic images, expansion of the photofluorographic principle to gastrointestinal surveying, and even such fundamental considerations as the deposition of lime salts and underlying causes of gastric and duodenal ulcerations.

The latter half of the volume is devoted to articles on Radiation Therapy and includes reports on effects of total body irradiation and of million-volt x-ray therapy. Many articles concerning carcinoma of the uterine cervix have also been included to familiarize the reader with the most recent data.

Much space is given to the use of I^{131} in treating hyperthyroidism and thyroid carcinoma. The sections on cancer of the breast and lymphoblastoma and leukemia are especially informative and well-written. The editors have selected their material so that the book is well suited for practitioners other than specialists in radiology.

N. S.

► RADIOLOGIC EXPLORATION OF THE BRONCHUS - - -

By S. DiRienzo, M.D., Assistant Professor of Radiology and Physiotherapy, Chief of the Radiology Department of the Institute of Cancer, The University of Cordoba, Argentina. Translated by Tomas A. Hughes, M D. 332 pages with 466 illustrations. 1949, Charles C Thomas, Springfield, Ill. $10.75.

This book constitutes an excellent detailed treatise on bronchography as formulated from the author's extensive experience with this method of examination. There is a preliminary discussion of the embryology, histology, and anatomy of the respiratory tract in the first three chapters which is intended to serve as a basic framework in the demonstration of pathologic anatomy and physiology later on.

It is in the fourth chapter that the central theme of the book is struck. The author makes clear his point that it is not only the anatomic characteristics of the bronchus which should be observed in bronchography but also the physiologic characteristics. He stresses the point that films taken after the filling of the bronchial tree do not help us fully appreciate the functional role of the bronchus or even the complete anatomic details. His method of examination is to obtain, during fluoroscopic examination while the opaque oil is being introduced, multiple serial films during various phases of filling and during various phases of respiration including coughing. In the further development of this idea, the author describes in detail the entire technic he employs including preparation of the patient, anesthesia, radiographic equipment, and assistants who participate as a team in the procedure of examination.

The author differentiates between "exploration of the bronchi" (which is essentially bronchography as practiced in this country) and bronchography in serial form which is the method he has developed and which he feels has certain indications often determined during the exploration. By means of serial bronchography he observes not only the anatomic abnormalities but also the pathologic physiology both of which, he feels, are essential in understanding the disease process. The use of this method of bronchography is exemplified in chapters dealing with bronchopulmonary malformations, bronchiectasis, emphysema and asthma, lung carcinoma, hydatid cyst of lung, and suppurations of the lung.

The author proves the value of his method of examination in many instances by case reports and a multitude of reproductions of excellent radiographs. There are a number of occasions in which bronchography appears to be overemphasized and unnecessary. In general, however, the worth of the method is well demonstrated, and a new aspect of bronchography is well developed.

L. G. R.

► DIAGNOSIS AND TREATMENT OF BRAIN TUMORS AND CARE OF THE NEUROSURGICAL PATIENT - - -

By Ernest Sachs, A.B., M.D., Research Associate in Physiology, Yale University, New Haven; Formerly Professor of Clinical Neurological Surgery, Washington University School of Medicine, St. Louis. Ed. 2. 552 pages with 348 illustrations and 10 color plates. 1949, The C. V. Mosby Company, St. Louis. $15.00.

This book is a combination of two previous publications of the author, namely "The Diagnosis and Treatment of Brain Tumors" and the "Care of the Neurosurgical Patient Before, During and After Operation." The author felt that these two subjects are so closely related that it might be wise to combine the two into a single publication.

In the first chapter there is a very fine description of external topography correlated with cerebral localization. Chapter 3 contains a very superficial discussion of the intracranial tumors. The descriptions of these lesions are very brief and many important tumors such as the mixed tumors, and many forms of meningiomas are completely omitted. The author refers to the astrocytomas as "cystic, well encapsulated lesions" disregarding the fact that most astrocytomas of the cerebrum are diffuse lesions which are difficult to remove.

Chapters 4 to 9 are devoted to a very brief discussion of diagnosis and differential diagnosis of brain tumors. In an attempt to simplify this most difficult subject, the author has made a number of statements that at present are still open to controversy and may be misleading to the young diagnostician.

The last half of the book includes a discussion of neurosurgical technics and the care of the neurosurgical patient. This material is clearly presented and well done. Chapter 9 is devoted to such general procedures as anesthesia, control of bleeding, subtemporal decompression, ventricular puncture, and the various types of neurosurgical exposures.

This chapter is followed by a large series of case reports to illustrate these operative procedures properly selected and used. The book is concluded by a good section on the postoperative care of the patient with some excellent suggestions regarding the care of the skin, bowels, bladder, as well as a discussion of postoperative fever.

The final half of this book dealing with the neurosurgical technics and the care of the neurosurgical patient is very well done and should be of value to the young student of neurosurgery. It tends to demonstrate to the physician the problems encountered in the neurosurgical handling of the patient. The early sections on diagnosis and histology of brain tumors are somewhat superficially handled and no doubt can be more accurately and better studied in a standard textbook of neurology.

A. B. B.

► FRACTURES - - -

By Paul B. Magnuson, M.D., F.A.C.S., Professor of Bone and Joint Surgery and Chairman of the Department, Northwestern University Medical School; and James K. Stack, M.D., F.A.C.S., Assistant Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago. Ed. 5. 537 pages, with 323 illustrations. 1949, J. B. Lippincott Company, Philadelphia, London & Montreal. $7.00.

Originally written to assist the physician who first attends the injured patient, this edition of "Fractures" begins with a chapter on fundamentals and carries that theme throughout the entire volume. The book is directed generally towards the practitioner with particular stress on the simple measures of treatment that are useful in all circumstances.

An interesting chapter, based on personal experiences of the authors, discusses the necessity of early reduction and maintenance in reduction of fractures presented for immediate treatment.

When the concepts of traction and countertraction are considered, any improvisation that accomplishes these measures is almost always successful and saves the patient from disabilities that may otherwise occur. This chapter, designated as the "farmyard" treatment of fractures, describes the emergency therapy of fractures and dislocations with mechanical devices usually obtainable in any farmhouse where necessary material is available. The approach to treatment is simplified as much as possible and is based on the anatomy, physiology, and functional anatomy of the muscles, bones, and joints.

The book does not go into operative procedures except to point out where surgical intervention by skilled operators might benefit the patient. Also it is useful as an aid to the practitioner in determining the prognosis of certain severe fractures that tend to produce unsatisfactory results. No evaluation of the various methods of treatment is debated in this volume as any new monograph on the subject recognizes that the basic nature and treatment of fractures remain the same as far as the present day knowledge is concerned. Suspension traction has been, and is still, established as the method of choice as determined from experiences in the past twenty years.

However, the material on compound fractures is brought up-to-date from experiences in World War II in the use of antibiotics as an adjunct in preventing infection such as osteomyelitis and other secondary complications. The various opinions on the use of skin grafts and the more recent findings relative to the immediate closure of wounds are also discussed.

The major portion of the book describes various fractures and their care with numerous prints of x-rays to illustrate results. Chapters on fracture dislocations of the spinal column and the skull have not been neglected. This portion was written by Dr. Loyal Davis and includes recent advances in that field. Improvements in the technics and application of physiotherapy are ably reviewed by Dr. John S. Coulter with an attempt to convey what one might expect as a final result.

H. O'P.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Breast Deformities and Their Repair. By Jacques W. Maliniac, M.D., Clinical Professor of Plastic Reparative Surgery and Associate Attending Plastic Reparative Surgeon, New York Polyclinic Medical School and Hospital, New York City; Attending Plastic Surgeon, Sydenham Hospital. 193 pages, with 119 figures. 1950, Grune & Stratton, New York. $10.00.

Primer of Allergy. By Warren T. Vaughan, M.S., M.D., Richmond, Virginia. Ed. 3, revised by J. Harvey Black, M.D., Dallas, Texas. 175 pages, illustrated. 1950, C. V. Mosby Company, St. Louis, Missouri. $3.50.

New Drugs *and* Instruments

Information published in this department has been supplied by the manufacturers of the products described.

CE-VI-SOL

PURPOSE: Water-soluble solution of vitamin C.

COMPOSITION: Each 0.5 cc. supplies 50 mg. ascorbic acid.

DOSAGE AND ADMINISTRATION: The usual daily dose for full term infants is 0.5 cc. May be stirred into feeding formula, fruit juice or other food, or dropped directly into infant's mouth.

HOW SUPPLIED: In 15 and 50 cc. bottles with dropper calibrated to dispense 25 mg. and 50 mg. ascorbic acid.

PRODUCER: Mead Johnson & Co., Evansville, Ind.

THEPTINE

PURPOSE: Antidepressant and restorative elixir.

COMPOSITION: Each 5 cc. (1 teaspoonful) supplies:

Dexedrine sulfate (dextro-amphetamine sulfate, S.K.F.)	2.5 mg.
Thiamine hydrochloride	5.0 mg.
Riboflavin	0.45 mg.
Niacin	6.7 mg.

In a wine-base vehicle containing 10 per cent alcohol.

INDICATIONS FOR USE: For patients in whom mental depression and nutritional inadequacy manifest themselves as apathy, lethargy, and physical debility.

DOSAGE AND ADMINISTRATION: Usual dosage is one teaspoonful (5 cc.) three times a day, after meals.

CAUTIONS: Use with caution in patients hypersensitive to sympathomimetic compounds; cases of coronary or cardiovascular disease which contraindicate vasoconstrictors; in presence of marked hypertension. Contraindicated in hyperexcitable or agitated prepsychotic states.

HOW SUPPLIED: In 12 fluid-ounce bottles.

PRODUCER: Smith, Kline & French Laboratories, Philadelphia, Pa.

THENYLENE—A.P.C.

PURPOSE: Antihistaminic drug for administration in the initial phase of the common cold.

COMPOSITION: Each capsule contains:

Thenylene hydrochloride (methapyrilene hydrochloride, Abbott)	25 mg.
Acetylsalicylic acid (aspirin)	230 mg. (3½ gr.)
Phenacetin (acetophenetidin)	150 mg. (2½ gr.)
Caffeine	30 mg. (½ gr.)

DOSAGE AND ADMINISTRATION: For adults—2 capsules as soon as possible after symptoms appear, then 1 or 2 capsules at intervals of three or four hours. Dose for children in proportion to weight.

HOW SUPPLIED: To be dispensed only by or on the prescription of a physician. In bottles of 100 and 500 capsules.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

MAXITRON

PURPOSE: All-purpose x-ray therapy machine.

DESCRIPTION: High radiation output makes possible the treatment of twice as many patients per day as equipment of earlier design. Use of a new-type tube with a beryllium window or exit port, permits treatment of conditions ranging from skin ailments, where nonpenetrating radiation is required, to deep-seated cancers which require highly-penetrating rays.

PRODUCER: General Electric X-ray Corporation, Milwaukee, Wis.

MURACIL—NEW NAME FOR ANTIBASON

Organon, Inc., Orange, N. J., has changed the name of its brand of methyl thiouracil from Antibason to MURACIL to conform with the nomenclature of the Council on Pharmacy and Chemistry of the American Medical Association. MURACIL has been accepted as the first brand of methyl thiouracil for inclusion in New and Nonofficial Remedies.

MURACIL (formerly Antibason) will continue to be available for physicians' prescriptions in 50 mg. tablets, bottles of 100 and 1,000 tablets.

THEPHORIN EXPECTORANT WITH CODEINE AND PAPAVERINE

PURPOSE: Treatment of cough associated with the common cold.

COMPOSITION: Provides Thephorin, codeine, papaverine, ammonium chloride, and chloroform. Cherry-flavored.

DOSAGE AND ADMINISTRATION: One or two teaspoonfuls one to three times daily for relief of cough.

HOW SUPPLIED: In 4-ounce and 16-ounce bottles.

PRODUCER: Hoffmann-La Roche, Inc., Nutley, N. J.

NESBIT OPERATING TABLE-CHAIR

PURPOSE: New A58-B Nesbit operating table and chair, adjustable to all positions needed for eye, ear, nose and throat work and general surgery.

DESCRIPTION: Unit is divided into three separate sections—the back, leg, and seat sections, which work in unison so the table can be changed to any position by a single control. The leg section may be dropped independently to a 90° angle. A hand lever elevates and lowers the top, a hand crank mechanism tilts the top. Footrest may be locked at right angles to leg section at any point along the side rails, dropped to form an extension, or completely removed.

Back and leg sections are welded angle iron frames covered with lead-coated sheet steel. Seat section is gray iron casting. The base is cast iron mounted on nickel-plated sliding floor-shoes.

Standard equipment includes a waterproof, leatherette-covered pad, adjustable headrest, and removable footrest.

Complete information available from:

PRODUCER: Ohio Chemical & Surgical Equipment Co., Madison, Wis.

NEO-FERINEX

PURPOSE: Treatment of secondary and certain nutritional anemias.

COMPOSITION: Each capsule contains:

Ferrous sulfate (exsiccated)	150 mg. (2.3 gr.)
Liver extract (Whipple fraction)	200 mg.
Thiamine hydrochloride U.S.P. (B_1)	1.0 mg.
Riboflavin U.S.P. (B_2)	2.0 mg.
Pyridoxine hydrochloride (B_6)	0.1 mg.
Calcium pantothenate	1.0 mg.
Niacinamide U.S.P.	5.0 mg.
Folic acid	0.5 mg.
Ascorbic acid U.S.P. (C)	20.0 mg.

Plus other factors of the B complex from liver extract.

DOSAGE AND ADMINISTRATION: Six capsules daily, preferably 2 capsules after each meal, or as directed by the physician.

HOW SUPPLIED: Bottles of 100, 500, and 1,000 capsules.

PRODUCER: The Paul Plessner Company, Detroit, Mich.

CREMOTRES

PURPOSE: Triple sulfonamide suspension.

COMPOSITION: Each 100 cc. contain:

Sulfamerazine	2 gm.
Sulfamethazine	4 gm.
Sulfadiazine	4 gm.

5 per cent alcohol and flavoring agents

INDICATIONS FOR USE: Treatment of infections in which sulfamerazine, sulfamethazine, or sulfadiazine alone is indicated.

DOSAGE AND ADMINISTRATION: Adults—initial dose of 2 tablespoonfuls followed by 2 teaspoonfuls every four hours. Children, 3 to 10 years of age—initial dose of 2 tablespoonfuls followed by 2 teaspoonfuls every six hours.

HOW SUPPLIED: Spasaver bottles containing 16 fluid ounces.

PRODUCER: Sharp & Dohme, Inc., Philadelphia, Pa.

AUREOMYCIN SPERSOIDS*

PURPOSE: Powder form of aureomycin, chocolate-flavored for ease of administration.

COMPOSITION: Provides 50 mg. of aureomycin per rounded (3 gm.) teaspoonful.

DOSAGE AND ADMINISTRATION: May be mixed with milk, water, other beverages, or food.

HOW SUPPLIED: In 75 mg. bottles (each bottle contains enough for 25 doses).

PRODUCER: Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

*Reg. U. S. Pat. Off.

GENTIA-JEL

PURPOSE: Vaginal moniliasis therapy.

COMPOSITION: Each applicator contains ¼ oz. of sterile jelly incorporating 0.2 per cent gentian violet, 3 per cent lactic acid, and 1 per cent acetic acid in a water-soluble base of polyethelene glycol.

DOSAGE AND ADMINISTRATION: One application daily until infection clears.

HOW SUPPLIED: Packages of 12 single-dose paper applicators.

PRODUCER: Westwood Pharmaceuticals, Buffalo, N. Y.

PANPARNIT®

PURPOSE: Reduction of rigidity and tremor in Parkinson's disease.

DESCRIPTION: Known previously as Parpanit, its essential action appears to be the blockage of proprioceptive impulses arising in muscles and joints, thus diminishing the intensity of the reflexes causing muscular rigidity in the parkinsonian syndrome.

DOSAGE AND ADMINISTRATION: Most satisfactory clinical results are obtained with careful individualized regulation of each patient's dosage.

HOW SUPPLIED: Sugar-coated tablets of 12.5 mg. and 50 mg.

PRODUCER: Geigy Company, Inc., New York, N. Y.

PASEM SODIUM

PURPOSE: Treatment of tuberculosis in selected cases.

COMPOSITION: A brand of sodium para-aminosalicylate (sodium 4-amino-2-hydroxybenzoate). A white crystalline powder, relatively stable when stored in dry form in amber bottles at room temperature.

DESCRIPTION: Inhibits growth of tubercle bacilli in vitro and vivo. It has no bacteriolytic properties and so does not kill the tubercle bacillus outright.

Sodium para-aminosalicylate is absorbed readily from the gastrointestinal tract. A single oral dose produces peak blood levels within the first or second hour after administration, but by the fourth hour blood levels drop appreciably.

DOSAGE AND ADMINISTRATION: The present consensus is that 6 capsules (0.5 gm. each) be given initially, repeated every three hours for a total of five doses each day (total of 15 gm. in twenty-four hours). However, dose should be adjusted to individual's response and tolerance. Treatment should be continued for a period of three to four months.

HOW SUPPLIED: In green-top capsules of 0.5 gm. each, bottles of 500.

PRODUCER: The S. E. Massengill Co., Bristol, Tenn.

ACON

PURPOSE: Prophylaxis and treatment of vitamin A deficiency.

COMPOSITION: Each cubic centimeter contains 25,000 units of vitamin A.

DOSAGE AND ADMINISTRATION: For oral administration by drop doses. Doses of 25,000 to 100,000 units daily can be used depending on individual requirements.

HOW SUPPLIED: 30 cc. dropper bottles.

PRODUCER: Endo Products, Inc., Richmond Hill, N. Y.

MUCILOSE COMBINED WITH CASCARA

DESCRIPTION: For patients who do not obtain sufficient stimulus from bulk laxatives alone, mucilose with cascara provides a mild yet effective treatment for constipation. A therapeutic dose starts evacuation in eight hours and remains gently effective until the bulk of mucilose passes through the large intestine, which requires a total of about thirty-six hours.

HOW SUPPLIED: Mucilose with Cascara Granules, in 4 ounce metal cans.

PRODUCER: Winthrop-Stearns, Inc., New York, N. Y.

DROP-CILLIN

PURPOSE: Oral penicillin expressly for "drop-dosage" to infants and small children.

DESCRIPTION: A stable dry powder which retains potency for eighteen months without refrigeration. In solution, Drop-cillin offers 50,000 units of penicillin G potassium in a dropperful (0.75 cc.).

HOW SUPPLIED: In 9 cc. bottles containing 600,000 units of penicillin. A dropper, calibrated to deliver approximately 20 drops (0.75 cc.), accompanies each bottle and is used by the pharmacist as the closure.

PRODUCER: White Laboratories, Inc., Newark, N. J.

REELEST TAPE RECORDER

DESCRIPTION: Features include twin-track recording without interruption for rewinding; patented Revers-A-Matic plays or records in two directions for one hour without attention; new Thred-A-Matic feature simplifies threading of tape; volume indicator—an electric eye called the Volumatic—for uniform recording. Design allows for playing of machine with top cover down, with all controls accessible. The Reelest is encased in a simulated leather case.

PRODUCER: Marketed by Universal Moulded Products Corporation, 1500 Walnut St., Philadelphia 2, Pa.

TIL-ZINE (TILDEN)

PURPOSE: Dual sulfonamide therapy.

COMPOSITION: Each fluid ounce contains:

Sulfadiazine	22½ gr.
Sulfamerazine	22½ gr.
Sodium citrate	45 gr.

DESCRIPTION: Peach-like flavored suspension of sulfonamides in microcrystalline form, producing rapid absorption and therapeutic blood levels in all indications amenable to treatment with sulfadiazine or sulfamerazine.

DOSAGE AND ADMINISTRATION: Adults—initial dose of 4 gm. (8 teaspoonfuls) followed by 1 gm. (2 teaspoonfuls) every four hours, day and night, until clinical improvement occurs and temperature remains normal for two days. Children—average daily dose of 0.25 gm. (½ teaspoonful) per kilogram of body weight (up to 65 pounds), one-third being given as initial dose followed by one-sixth of the total daily dose at four-hour intervals.

HOW SUPPLIED: In 4-ounce and one pint bottles.

PRODUCER: The Tilden Company, New Lebanon, N. Y.

Consultation Service

This special consultation information service is offered as a regular monthly feature of *Postgraduate Medicine*. Readers are invited to call on this Service for answers to difficult medical problems from our consultants and members of our Editorial Board best qualified to help. Each question will be answered by mail and those of general interest will be published each month. Address all communications to Consultation Service, *Postgraduate Medicine*, 516 Essex Building, Minneapolis 3, Minnesota.

TOXEMIA IN PREGNANCY

QUESTION: I have a patient who is anxious to become pregnant, but she has a history of toxemic albuminuria in her first pregnancy. At present, she is free from symptoms; would it be advisable for her to become pregnant again?

M.D.—Nevada

ANSWER: In deciding whether pregnancy should be avoided in the case of a woman who has had a presumable toxemia in her most recent pregnancy the most essential factor is the residual damage in the kidney. In most cases there is no discoverable renal or arteriolar damage, and pregnancy can safely be undertaken. In some cases there is an obvious residual nephritis, and pregnancy should be avoided or terminated if it occurs. Between these extremes there are two major gradations of renal-vascular damage:

1. The apparently normal kidney without hypertension which develops nephritis during the course of pregnancy. When this occurs early in pregnancy, termination of the pregnancy and sterilization are indicated. In late pregnancy the decision in favor of the fetus requires exact information and a great deal of judgment—the pregnancy should be terminated when the fetus has reached a reasonably safe viability, as many of these babies die in the last two weeks of pregnancy.

2. In the case of hypertension without evidence of renal damage, the principles are the same—many of these represent obstetrically insignificant types of hypertension. In all cases blood-chemistry studies and renal function tests should be carried out, although positive or negative action should not be based upon the latter alone.

WILLARD R. COOKE

TREATMENT OF KIDNEY DISORDERS

QUESTION: Throughout my general practice of medicine I have been called upon to treat quite a number of cases of kidney disorder. I hope that your answers to this one case will aid me in treating this and other such cases.

A white woman aged 28 suffered a miscarriage some seven months ago. General tiredness, bodily swelling, four-plus albumin, casts, and blood cells all appeared during her pregnancy. The swelling disappeared shortly after the miscarriage but the albumin, blood cells, and casts have remained. These urine tests have been run an average of four times a day for six months. The quantity of albumin present varies greatly. Tests taken only a few hours apart will vary from a mere trace of albumin to a four-plus. The average of the tests seems to improve each month. The tests are the lowest—and at times perfectly clear—during menses. The patient has been placed on a salt-free diet, moderate rest, and vitamins.

What can be done to discover how much the kidneys have been damaged and whether such damage is permanent? How can one find whether the damage is in the upper or lower tubular region? Does the liver have an important effect on such cases? What possible meaning can be drawn from the clear tests during menses? What is the effect of penicillin, streptomycin, and sulfas in the treatment of such kidney disorders? What treatment would you recommend for the above case?

M.D.—Ohio

ANSWER: The history of this patient as presented immediately raises the question as to whether her present condition is the result of her pregnancy, or whether she may not have had previously unrecognized chronic glomerulonephritis. The present picture suggests chronic glomerulonephritis or chronic diffuse nephritis secondary to some other pathologic process.

The urea clearance test or the serum sulfate determination is the most readily available test to indicate whether or not there is appreciable damage to the kidneys. No test is of much value in determining the permanence of damage, but renal impairment that exists over a period of many months usually is permanent. There are no satisfactory tests to indicate whether the damage is in the upper or lower tubular region. In most instances of renal damage, there are changes in both glomerular and tubular portions of the nephron.

When a patient has albuminuria, there frequently are wide variations in the amount of albumin excreted. The level of physical activity is an important determining factor.

Benefit would not be expected to follow the use of chemotherapeutic agents. There is no efficacy in a "salt-free" diet in such a case, in which edema has disappeared. The program of choice, in the absence of azotemia, would be moderate activity, avoidance of infection, and general hygiene.

DIAMOND REPLACEMENT BLOOD TRANSFUSION

QUESTION: Could you give details as to the technic of the Diamond replacement blood transfusion in congenital hemolytic disease. References are difficult for me to obtain but several would be helpful for record purposes.

M.D.—Alberta, Canada

ANSWER: The technic of replacement blood transfusion in the treatment of hemolytic disease of the newborn is generally as follows: the stump of the umbilical cord is cut about 6 inches from

(Continued on page A-50)

1/2 cc.

Improved Cutter Pediatric Toxoids, Alhydrox* or plain, are now more highly purified. Increased potency reduces the dosage volume one-half, and gives the same high immunities you have always obtained with Cutter Toxoids. Write for immunization schedule. Cutter Laboratories, Berkeley, Calif.

* *Trade name for Aluminum Hydroxide adsorption, exclusive with Cutter. Alhydrox, added to proven, potent biologicals, results in a solid immunity and less pain on injection.*

the baby's navel at birth. At the time of transfusion, the cord is again cut, about 1 inch from the abdomen. A flexible plastic catheter is inserted into the umbilical vein for a distance of 10 to 15 cm. until a free flow of blood is obtained. Because of the tortuous course of the umbilical vein, care must be exercised in introducing the catheter.

The catheter is attached to a 10 or 20 cc. syringe by way of two three-way stopcocks—the one nearest the catheter being connected to a 250 cc. bottle such as is used to hold solutions for intravenous use. The other end of this three-way stopcock is connected by rubber tubing to the second three-way stopcock, which is in turn connected to the 10 or 20 cc. Luer-Lok syringe and to the Erlenmeyer flask containing the donor's blood (Rh-negative).

Blood is withdrawn from the infant in quantities of 10 cc. and is discharged into the exhaust bottle. A squirt of heparin is made into the exhaust system by the syringe at this time to prevent clotting of the blood in this system. After 20 to 40 cc. of blood has been removed from the infant, a similar quantity of Rh-negative blood, group 0, is infused without heparin by suitable arrangement of the three-way stopcock. Injection is made slowly. This is continued until an amount of blood has been injected that is slightly more than the baby's calculated blood volume (70 cc. per kilogram of body weight).

References which explain the method in greater detail and with variations are appended.

REFERENCES

1. Arnold, D. P., and Alford, K. M.: A new technique for replacement transfusion in the treatment of hemolytic disease of the newborn infant. J. Pediat. 32:113-118 (February) 1948.
2. Diamond, L. K.: Erythroblastosis foetalis or haemolytic disease of the newborn. Proc. Roy. Soc. Med. 40:546-550 (July) 1947.
3. Platou, E. S., Heilig, W. R., Bergan, R., and Tudor, R. B.: Exchange transfusion; new method of treatment for erythroblastosis fetalis. J. Lancet 67:180-184 (May) 1947.
4. Wallerstein, H.: Substitution transfusion: new treatment for severe erythroblastosis fetalis. Am. J. Dis. Child. 73:19-33 (January) 1947.

DIAGNOSIS OF HODGKIN'S DISEASE

QUESTION: Can you make a diagnosis of Hodgkin's disease merely by doing a biopsy of bone marrow? I thought a gland was necessary for biopsy. My patient has anemia, enlarged spleen, and marked pruritus. Diagnosis in a large clinic was made after biopsy of sternum. This was two years ago and there are still no palpable or mediastinal glands. What do you think?

M.D.—Newfoundland

ANSWER: Hodgkin's disease fundamentally involves the reticular tissue of the reticuloendothelial tissue and therefore, as should be expected, it often involves bone marrow where the lesions may be demonstrated by actual biopsy, although rarely by simple aspiration of bone marrow. Superficial lymph nodes need not be affected. Cases have been reported in which autopsy revealed the lesions of Hodgkin's disease to be confined to the bone marrow and spleen, or bone marrow and liver.

R. LEE CLARK, JR.

VITAMIN E QUESTIONABLE IN TREATING HEART CONDITIONS

QUESTION: In Canada at the present time there is considerable controversy over the merit of vitamin E in the treatment of chronic heart conditions. The Shutes of London have published startling results from this treatment but various tests by other workers in the medical schools and in some of the larger hospitals have showed negative or indifferent results.

Vitamin E treatment for cardiac cases has had considerable publicity in the newspapers here and numerous patients becoming discouraged with results of standard cardiac treatment have been pressing for the trial of vitamin E.

I would appreciate it if you would inform me what you consider the status of vitamin E therapy to be in cardiac cases.

I have read considerable literature concerning this subject and can see little in its favor from recognized medical authorities and up to the present have been discouraging patients in its use.

M.D.—Ontario

ANSWER: Vitamin E is a mixture of alpha, beta, gamma, and delta tocopherols. The tocopherols are widely distributed in nature, being found particularly in vegetable oils and green leaves. The therapeutic effects in cardiac and other disorders have been attributed principally to the alpha tocopherols.

The recommended daily dose of 200 mgm. or more of alpha tocopherol considerably exceeds that necessary to correct a deficiency. Actually, the advocates of vitamin E therapy in heart disease have not claimed that their results were due to correction of a deficiency, but have attributed them to some unidentified pharmacologic action. Dilatation of small blood vessels and alteration of intracellular oxidation have been suggested as mechanisms, but the proof has not been too convincing.

It does not appear likely that one agent would affect such diverse conditions as acute rheumatic fever, coronary insufficiency, and congestive failure. A review of the papers attesting to the beneficial effects of vitamin E hardly leads to the enthusiasm exhibited by the authors. Noteworthy is the uncritical manner in which the cases are presented, particularly the failure to take into account the natural history of the cardiac disturbance under consideration.

The complete lack of successful or even promising results reported by so many investigators leads to the conclusion that the value of vitamin E in the treatment of heart disease has not been proved.